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**AN INTRODUCTION TO
ANIMAL PHYSIOLOGY**

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PLATE I. TOADS WITH THEIR CHROMATOPHORES IN DIFFERENT STATES

The two had been under similar conditions for an hour before they were photographed, except that the dark one was on a black background and the light one on a white background. They were placed together on a white background for photography.

AN INTRODUCTION TO
ANIMAL
PHYSIOLOGY²

BY

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OXFORD
AT THE CLARENDON PRESS

*'Come, tell me how you live,' I cried,
'And what it is you do.'*

THE WHITE KNIGHT.

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PREFACE

I AM well aware that in attempting to cover in one elementary volume almost the whole range of animal physiology, I am treading on ground where no English angel has been before me. I wish that it were otherwise, for the scope of physiology is so vast that few men can claim personal acquaintance with more than one or two small parts of it, and the risk of error is great. But in the country of the blind the one-eyed man is king, and I have written this book with the object of giving students a fuller and more accurate account of animal physiology than is at present available. As far as possible I have tried to base my material on original papers, but at many points I have had to rely on the more recent larger text-books of physiology and biochemistry. Only very occasionally, however, have I made use of any book which did not give references to original work, and I hope that in this way mistakes have been reduced to a minimum. Nevertheless, in a text-book on a rapidly developing subject, error is inevitable. I should be grateful to readers who will point out mis-statements, but I would ask them to give references, or better still (if they should be research workers) to send reprints.

The book was written not for examination requirements but because I believe that young zoologists should know more physiology than they usually do. Nevertheless, it will, I hope, be useful for the First M.B., Higher School Certificate, and College Scholarship examinations, for all of which an increasing knowledge of physiology is demanded. In addition it should serve for junior University students.

No author could have been more fortunate in his helpers than I have been. To all of them I offer my thanks, but especially to Dr. G. R. de Beer and Mr. P. F. Haggart, both of whom read the whole manuscript and left it better

than they found it; to Mr. C. W. Carter for reading the book in proof; to Mr. J. Z. Young for reading section V, and to Professor C. M. Yonge for reading most of section I; to Professor J. H. Orton, Professor A. D. Ritchie, Mr. H. Lob, Mr. D. M. Hall, and Mr. E. G. MacGregor for advice on particular points; and to Mr. William Holmes for advice and for assistance with the Index.

Lastly, I must record my thanks for the great help I have received from the officials of the Clarendon Press.

W. B. Y.

MANCHESTER,

December 1938.

NOTE

THE war has prevented any major alterations in this impression, but a number of statements of fact and a few misprints have been corrected, so that I hope that although three years have passed since the writing of the book was finished, it will still be found to be a reasonably up-to-date account of animal physiology. The highest density of alteration will be found in the sections on vitamins and hormones, subjects in which research is extensive and rapid. The general outlook of these parts is now to a great extent old-fashioned, and I hope that at some future time it will be possible to improve them considerably. Meanwhile, I have tried to amend them so that they are not misleading.

My thanks are due to correspondents who have pointed out errors and to critics who have suggested improvements. I have sometimes been prevented from adopting the latter, but I am none the less grateful.

W. B. Y.

MANCHESTER,

August 1941.

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INTRODUCTION

EVERY elementary student of biology learns that his subject is divisible, as it might be vertically, into botany and zoology, and horizontally into morphology and physiology. Of the latter division as applied to plants he sees much, but his knowledge of animals tends to consist for a long time of only the structure of their parts, with which the names of certain rather ill-defined functions are connected. In the present book an attempt is made to explain these functions more fully, and in so doing to give an account of the way in which an animal, considered as a machine, works. This is very much the same thing as describing what it does and how it does it, provided that the peculiar acts of individuals are neglected. As far as possible even species are neglected, and statements are made as general as possible. Of course, in experimental work particular individuals and particular species must be used, and the latter are often named in the text, but in practice there are usually only minor differences in the physiology of all the members of one class; we are most interested in the generalizations made inductively from particular observations.

In addition to a certain amount of intelligence and common sense, two things are assumed in the reader; some knowledge of biology as usually taught for the Higher School Certificate or First M.B. examinations, and a similar knowledge of chemistry. The first is not likely to be lacking, and, indeed, if it is this book is useless, for physiology must be based on a sound knowledge of morphology. A few anatomical structures which are frequently neglected in the books are described or illustrated, but no attempt is made even to remind the reader of things with which he should be familiar. Unfamiliar names or points

of classification should be looked up in one of the ordinary zoology text-books as they occur. Similarly with the biochemistry it has been assumed that so much of this subject as is usually taught for the botanical side of First M.B. biology will be available to the reader in books even if he does not remember it. In a few places a knowledge of physical chemistry possibly above that of the examinations mentioned will be useful. Such parts must be skipped by those who cannot understand them; they have been inserted because for those who can follow them they make the physiology clearer and easier.

The book proper begins with a section called Nutrition. This deals with the food which an animal needs, how it gets it, and what it does with it in order to be able to absorb it; the absorption itself, and the intermediate metabolism, that is, the way in which the food is built up to become part of the body. The next section, Excretion, deals with the elimination of waste products, and so finishes the story of what happens to the food, although a big gap has been left in the middle. The third section is called Respiration, rather inadequately, for it deals with much more than what is sometimes understood by that word. It includes the means by which energy is provided for the animal, and, since most energy is obtained by oxidation, a good deal about the oxygen supply.

That finishes the more narrowly chemical side of physiology. The fourth section, Effectors, describes those tissues which do things in the sense of having an effect on the outside world—muscles, glands, cilia, and so on. Next comes Co-ordination, dealing with the methods by which the processes described in the other sections are kept running in such a way that the animal reacts as an individual, and not as a vast number of independent units. This section includes divisions on nerves, hormones, and sense organs. The sixth section is called Behaviour, and tries to

show, without being dogmatic as to metaphysics, that much of what the animal does as an individual can be usefully studied from the same mechanistic standpoint as are its isolated parts in the traditional physiological laboratory.

After that comes a section on Reproduction, which needs no explanation, and lastly a short section dealing with some of the ways in which the higher animals have become independent of their environment.

I

NUTRITION

THE food of animals is used in two ways, as a fuel to supply energy, and as raw material to be incorporated in the tissues of the body. In the second case it may be used to make completely new material (growth in the strict sense) or it may merely be used for repair of structures broken down in the life processes of the organism. The animal must first obtain raw material (feeding); this must be prepared for absorption (digestion), and after it has been absorbed it must suffer chemical changes according to the purpose to which it is to be put. In the present section these processes will be treated in order. The final break-down of the substances which provide energy, and the disposal of the waste products, will be dealt with in the chapters on Respiration and Excretion respectively.

1.1. The Foodstuffs, their Nature and Source

Since the ultimate chemical analysis of any animal is always approximately the same, it follows that certain elements must be present in the food. A full list of those necessary for any species is probably at present impossible, but careful analyses and feeding with rigidly purified food have shown that many more than the common half-dozen or so biological elements are required. In some cases animals are very efficient in obtaining particular elements from their food. The tunicate *Ciona* has in its blood a protein which is rich in vanadium, yet this substance has never been detected in the sea-water in which the animal lives. Nearly all marine arthropods and molluscs possess haemocyanin, which contains copper, the concentration of which in sea-water is 1 part in 10⁹. Some Protozoa (*Radiolaria Acantharia*) form shells of sulphate

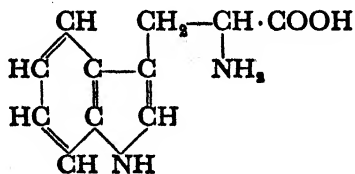
of strontium, an element which again is scarcely present in the sea. These facts have led a few people to suggest that the animals concerned can transmute the elements, but this is hardly likely.

It is in many cases necessary not merely that a certain element be present in the food, but that it be present in a particular form of combination, and this is strikingly the case for the elements which are required in the greatest proportion, that is for carbon, hydrogen, and nitrogen. Taking account of this, it is convenient to divide the food of animals into the following classes:

Proteins
Fats
Carbohydrates
Other organic compounds
Inorganic substances.

1.11. Proteins

Proteins make up an essential part of protoplasmic structure, and in the normal way the food from which they are derived consists also of proteins. These are all broken down to aminoacids before absorption, and it would therefore be expected that the latter could be used instead. This is the case, but since not all the aminoacids can be converted one into another it is necessary that certain quantities of particular acids be present. This is largely because the animal needs certain ring groups which it cannot synthesize, and these are only supplied in proteins. Tryptophane, for instance, which has the formula



cannot be synthesized by animals, and it must therefore be present in the food, either free or combined as a protein. For the same reason proteins are not all of equal value, since varying amounts of them are necessary to supply the required aminoacids. Maize, for instance, contains no tryptophane, and is in consequence an inadequate food. Speaking generally, less protein is needed if it is of animal origin than if it comes from plants. Proteins which contain most of the necessary aminoacids in proportions suitable for animals are called first class, and while most animal proteins are in this group (gelatin is a notable exception) it includes but a few vegetable proteins. Mammals do not store protein to more than a very slight extent, so that in the adult most of the nitrogen in the food soon appears in the urine. Accordingly a continual supply of protein is necessary. The minimal quantity seems to vary with the other food and with the past history of the subject.

There is no evidence that any animals other than the photosynthetic green flagellates, whose metabolism is that of plants, can live on food which is lacking in aminoacids, though some nitrogen may be obtained from other sources. From time to time revolutionary claims have been made that certain species can live on such a diet, but in all cases it has later been shown that symbiosis with plants was taking place. *Drosophila* larvae can live on mineral salts, sugar, and ammonium tartrate ((CHOH·COONH₄)₂), but if they are carefully cleared of the yeasts which are normally present in the gut, they die on this food. The ciliate *Colpidium* was thought to be able to live on ammonium glycerophosphate,



but it was found that Bacteria were present. Termites live symbiotically on *Trichonympha* and other flagellates which live in the gut; they can grow successfully when fed only

on the purest filter-paper, which contains but 0.0006 per cent. of ash. The source of the nitrogen in this case remains a mystery. As shown later (p. 37), mammals can manufacture aminoacids from ammonia, and rats can utilize ammonium ions present in the food.

1.12. Fats

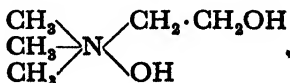
Fats are an important constituent of most foods, and it seems that in the mammal some of the energy must be supplied from this source in normal life. Moreover, fatty acids in the form of phospholipides such as lecithin enter intimately into protoplasmic structure. Nevertheless, fats can be formed from carbohydrate, and in animals such as those Protozoa which digest fat scarcely at all this is the source from which the protoplasmic fat presumably comes. In fly larvae, fat is formed from protein, but it appears unlikely that this occurs in the mammal.

1.13. Carbohydrates

Carbohydrates are in most animals the chief source of energy, and although they can be formed both from fat (p. 44) and from protein (p. 38) a certain amount, which differs for different species, must be present in the food. Carnivores need less than herbivores. In mammals absence of carbohydrate upsets the fat and protein metabolism.

1.14. Other Organic Compounds

In addition to the three main classes certain other organic compounds are required. One of these is choline,



a base which enters into the lecithin molecule and is also important in nervous stimulation (section 5.32). The vita-

mins, of varied composition, belong here, but they are so important as to deserve a section to themselves (pp. 46-54).

1.15. Inorganic Substances

Besides the oxygen required for respiration certain other compounds and elements are necessary. Water, although it is formed in small quantities in the body by oxidation of organic materials, is lost in far larger quantities by evaporation and in urine and faeces. The deficit must be supplied in food and drink, and in man six-sevenths of the daily loss must be obtained in this way. In small terrestrial animals, particularly insects, the control of water loss is very important, as it is one of the most difficult foods to supply. Salts such as sodium chloride are necessary for the efficient functioning of most organs, and must be supplied in the food. The majority of the elements which in small quantity are necessary for life and growth are probably supplied in the form of inorganic ions.

1.16. The Food Requirements of Man

The normal food requirements of man depend in part on the amount of external work which he does, but even when this is reduced as near to zero as possible some energy, and so some food, is still required. The heart and some other organs are working continuously, and energy is lost in the form of heat. The energy output of a fasting resting animal which is doing no external work is called its basal metabolism. When this is calculated per unit of body-weight it is found to be greater the smaller the animal. This is to be expected, for the smaller an animal the higher is the ratio of its surface to its volume, and so the more rapidly does each gramme of it lose heat. If basal metabolism is calculated per unit of area of body-surface, it is found to be fairly constant for a given species. In men it is about 40 Calories per square metre per hour, and

it is about 2·5 Calories less in women. The heavier a man is the higher will be his basal metabolism, but small men have a greater energy output per pound. If minor differences in shape are neglected it is possible to construct a nomogram connecting surface with height and body-weight, and from this the basal metabolism of any man for whom the usual physical dimensions are known can be calculated. The average height of Englishmen is 171 cm. (5 ft. 7 in.) and weight 70·3 Kg. (11 stone). This corresponds to a surface area of 1·8 m.², which gives a basal metabolism of 71 Calories per hour. When allowance is made for the increased metabolism when the man is up and about, and for an average amount of external work, the energy requirement comes to about 3,000 Calories per day. There can of course be no exactness to this figure, since it is at best an approximate mean. Men in sedentary occupations will need less, those doing heavy manual labour, more. A tailor has been calculated to need but 2,500 Calories, and a woodcutter as much as twice this. Women need about four-fifths of what a man does, and children still less, according to their size.

There is quite a large loss in cooking so that a total of about 3,400 Calories a day must be supplied in the food. There seems little doubt that a surprisingly high proportion (10 per cent.) of the population of Great Britain is on this basis undernourished. Further, as has been said above, it is necessary for a healthy life that some of the energy should be supplied from fat and some from protein, although men have succeeded in living on diets very low in both of these. In England not less than 10 per cent. of the energy should be supplied by protein, of which half should be first class, and a quarter should be supplied by fat. This means that at least 70 gm. (2·5 oz.) of protein should be taken per day, a standard which again is not reached by a tenth of the population. The need for in-

creased protein for growing children, who are forming new protoplasm, is obvious. The proportion of the population which does not get an adequate supply of vitamins and some of the more important inorganic substances is possibly as high as one-half.

1.2. Feeding and Feeding Mechanisms

The method by which an animal obtains its food depends on the class to which it belongs, and also, and even more, on the nature of its food. On the latter basis it is possible to divide animals by their feeding mechanisms into three or four main types:

- Microphagous feeders
- Macrophagous feeders
- Detritus feeders
- Fluid feeders.

1.21. Microphagous Feeders

Microphagous feeders are animals which live on small particles, usually plankton. It is a characteristic of these that they scarcely ever stop feeding, and they are often, though by no means exclusively, sedentary or sluggish. Perhaps the commonest method which they use is to draw a current of water to the mouth by means of cilia, food particles being abstracted and the water expelled. This is found in nearly all phyla from the Protozoa to the chordates (with the obvious exception of the nematodes and arthropods, which possess no cilia). The long cilia in the oral groove of *Paramecium* draw a cone of water towards the cytoplasmic mouth, and food particles thus brought into contact with this are ingested. Some sea-anemones, such as *Metridium*, are covered with cilia which may beat towards the mouth, to which they convey plankton. Normally they beat in the opposite direction, so that waste products are removed, this being one of the few cases where reversal of cilia undoubtedly takes place. In the

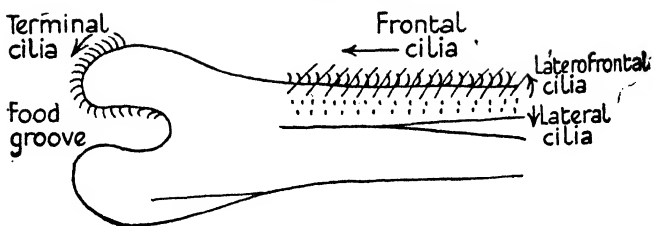


FIG. 1 A. Diagrammatic lateral view of *Mytilus* gill filament. Modified from Orton.

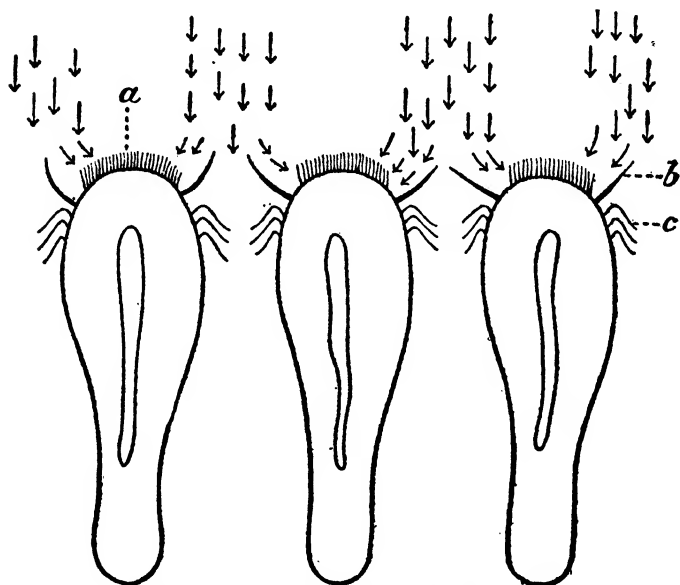


FIG. 1 B. Transverse section of three gill filaments, showing the deflection of the vertical current on to the frontal cilia.

a. Frontal cilia; b. laterofrontal cilia; c. lateral cilia. After Gray.

lamellibranchs there is a complicated arrangement of cilia on the gills, palps, and mantle, by which a current of water is brought into the shell, particles of a certain size

selected and carried to the mouth, and water and waste material ejected. In the sea-mussel *Mytilus* an outline of what happens is as follows. The inhalant current is caused by cilia on the gills. On the gills there are cilia in three positions (Fig. 1). The lateral cilia cause an inward current directed on to the gills, and the particles carried in this are diverted by the laterofrontal cilia on to the edge of the gill filaments. Here the frontal cilia carry them down to the groove in the free edge of the gill, where they are carried forward to the palps. On these there is mechanical selection of particles by size. A simplified section of a palp of an oyster is shown in Fig. 2; light particles are thrown over the tops of the ridges and go to the mouth, while heavy particles fall into the grooves and are taken to the edge of the palp. Cilia on the mantle cause a current which takes these rejected particles, together with other waste products, to the *inhalent* siphon. In some species muscular contraction of the gills and palps helps in the transport of the particles. The most advanced form with ciliary feeding is the ammocoete larva of *Petromyzon*.

There are other types of microphagous feeding. In some species of Crustacea setae on various appendages are used to create a current of water, and the larva of *Culex* feeds so efficiently in this manner that it is said even to be able to feed on colloidal particles, though it cannot get enough of them to grow.

1.22. Macrophagous Feeders

Macrophagous feeders are those which feed on comparatively large masses of food, and which in consequence only feed occasionally. Examples, from the Protozoa to man, are fairly obvious. The Rhizopoda ingest particles of food in a number of ways. In some (e.g. *Amoeba proteus*), water is taken in with the food, so that a vacuole is formed at

once, while in others (e.g. *Actinosphaerium*) the food is taken practically dry, and water is then secreted round it. The food particle may simply be drawn into the cyto-

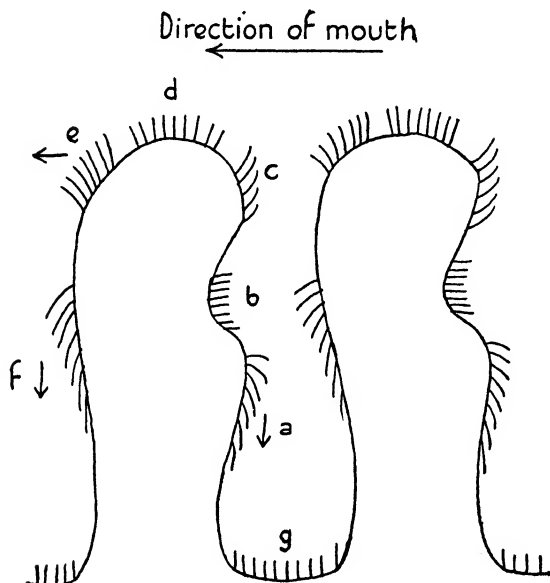


FIG. 2. Diagrammatic section through two ridges on the palp of an oyster. The whole palp is covered with cilia, but for clarity these are shown in seven separate blocks according to their direction of beat. Blocks *a*, *e*, and *f* beat in the direction shown by the arrows; block *b* through the plane of the paper towards the base of the palp; block *c* diagonally towards the mouth; and blocks *d* and *g* through the plane of the paper towards the upper margin of the palp. Reconstructed from Yonge.

plasm, the whole animal may flow round it, or two definite pseudopodia may be used to surround it. The last is the method normally used by *Amoeba proteus*. *Amoeba* can cut a paramecium into two pieces. All the Hydrozoa, although they move very little, are nevertheless macro-

phagous, animals which happen to touch the tentacles being paralysed by the nematocysts. The threads of these can penetrate even through chitin. The tentacles carry the prey to the mouth, and in *Hydra* as soon as the latter is touched they withdraw. *Hydra* has been described as stretching itself over its food 'like a serpent or an automatic stocking'.

In macrophagous forms the food has often to be broken up before the digestive enzymes can act on it, or even before it is taken into the mouth. Occasionally there is very vigorous external digestion. The protozoan *Vampyrella* pours out a cellulase to dissolve the wall of the Alga *Spirogyra* on which it feeds. The starfish *Asterias* extrudes its stomach over its prey, such as a mollusc, and a considerable amount of digestion takes place before the food is swallowed. A number of species inject a protease into living animals. Most of the cephalopods do this, and so do the larvae of the beetles *Dytiscus* and *Lampryis* (the glow-worm). The first of these insects lives on almost any living thing which it can catch—tadpoles, for instance—and the second on snails and slugs. Spiders likewise inject proteases into the flies which they have caught. In their case the external digestion is so complete that the food actually taken into the body is liquid, and any parts not dissolved are rejected.

More often the food is broken up by mechanical means. In decapod Crustacea such as *Potamobius* (*Astacus*) food is first torn by the chelae, and then pulled to pieces by the endopodites of the second and third maxillipeds while being held in the mandibles. After it has been taken into the mouth it is further broken up in the gizzard, a special part of the foregut bearing internal teeth or pyloric ossicles. Insect jaws and palps are used to the same purpose as the mouth-parts of Crustacea, and species which feed on hard food (Coleoptera, Orthoptera, some Hymenoptera) have

well-developed mandibles. The radula of such gastropods as the snail is used for cutting pieces of leaf of suitable size; for this purpose it works against a hard pad on the roof of the mouth. For the most part the lower vertebrates swallow their food whole: this is the case in the dogfish, where whole crabs may often be found in the stomach, and in the frog and snake. The egg-eating snake *Dasyveltis scabra* has an interesting special adaptation. The haemal spines of the cervical vertebrae project into the oesophagus, and as the egg is pressed against them while it is being swallowed, its shell is broken. Most birds also swallow their food whole, though parrots break it up very finely with the beak and tongue, and thrushes and some shore birds break the shells of molluscs before eating them. The gizzard is very muscular, but has no hard parts; instead, it contains small stones which have been swallowed. Food is crushed by being worked against these. In mammals, the teeth, in addition to being used to seize the food, may also serve to crush it in the mouth. In accordance with this the type of food has a close connexion with the form of the teeth, particularly of the cheek teeth. The molars of carnivores have cutting edges, but are not used for grinding: those of herbivores have ridges, and of omnivores rounded cusps, both being suited to chewing. Animals which live on small invertebrates, badly called insectivorous, have cheek teeth with sharp points. Piscivorous species do not chew their food, and have simple conical molars adapted for holding their prey.

1.23. Detritus Feeders

Detritus feeders, those which feed on the organic matter in soil and mud, are perhaps best placed with or near macrophagous forms. They include burrowing species like *Lumbricus*, those which shovel sand into the mouth like the holothurians, and a few such as the sturgeons which

suck mud with the lips. In all cases in order for the animal to get enough food a great deal of useless mineral matter has to be passed through the body.

1.24. Fluid Feeders

There remain several species which feed on food which is already liquid. Most of these suck fluid through some sort of mouth apparatus. The majority of them are insects. The chief free-living forms are Lepidoptera, bees, and blowflies, which have three different types of sucking apparatus developed from the mouth-parts. The ectoparasitic insects such as bugs, mammal lice, and mosquitoes also mostly get their food in this way, but here the mouth-parts are capable not only of sucking but of first piercing through the epidermis of the host. Ectoparasites of other classes, such as ticks and leeches, use a similar method. Both of these last groups have been shown to produce an anticoagulin to prevent clotting of the blood while it is being sucked. A few endoparasites also use this method: the liverfluke lives mainly on bile which it draws in through the mouth, which is surrounded by the anterior sucker, and some nematodes such as *Ankylostoma* browse on the mucous membrane of the gut wall and obtain much blood (Fig. 3).

The more extreme endoparasites, such as the Sporozoa, Cestoda, and *Sacculina*, absorb food over practically the whole body-surface. It has been suggested that free-living animals might be able to absorb organic matter directly, either through the gut wall or through the outer surface. There is some circumstantial evidence for this, such as the fact that although Leptocephali larvae of the eel live and grow in the Atlantic for three years little food has ever been found in them; but it is unlikely that the small amounts of organic matter in either fresh or sea water (10 mg./litre) can ever be very important.

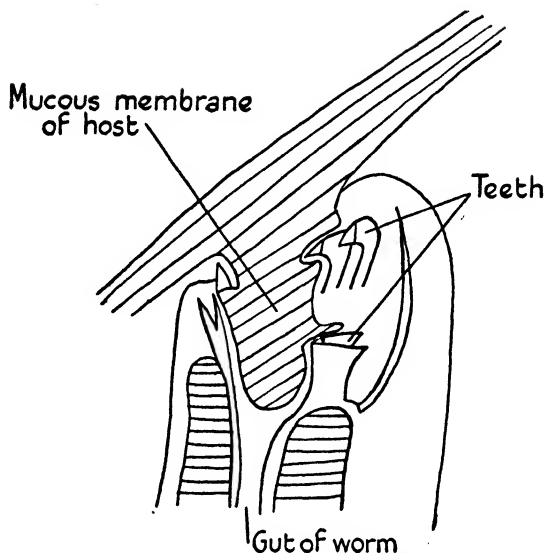


FIG. 3. Diagrammatic L.S. of anterior end of *Ankylostoma* attached to the wall of the gut. In part after Brumpt, *Précis de Parasitologie*, Masson et Cie, in part after Keilin.

1.3. Digestion

It is characteristic of animals that much of their food consists of complex organic substances, which are chemically relatively inert and often insoluble. They cannot be directly used for the metabolism of the body, but must first be broken down into simple diffusible products. Such preparation of the food is called digestion. The products must not only be soluble, but they must also be such as the body-cells can absorb and deal with. A further need for digestion lies in the fact that, even if the food is soluble, it is of a different nature from the tissues of the body. All proteins are made up of combinations of relatively few aminoacids, but one protein cannot be converted to another unless it is first broken down to its constituent

aminoacids. A protein molecule is like a model made of a constructional toy in which the strips of steel of different sizes represent different aminoacids. An aeroplane and a saw-mill may consist of nearly the same aggregate of parts, but they are arranged in different ways, and the one can be converted into the other only by being first completely dismantled. The sugars are similar, and even disaccharides, though crystalline and diffusible, must be broken down to monosaccharides before the cells can use them.

Digestion is generally carried out by enzymes, and in nearly all cases the chemical action they catalyse is a hydrolysis. In the majority of animals the enzymes are secreted into the gut, so that digestion is internal but extracellular. External digestion has already been dealt with under feeding mechanisms (p. 11). Intracellular digestion, in which enzymes act on substances already in the cells, is normal in Protozoa, sea-anemones, Platyhelminthes, and lamellibranchs. It is possible that it takes place in the vertebrate small intestine, various enzymes acting on preliminary soluble break-down products formed in the gut lumen. An enzyme is always affected by the acidity of the medium in which it is acting, and optima have been measured in many cases. The exact values, however, seem to vary according to the degree of purity of the enzyme, and according to the salts and other substances present. It is therefore only possible to indicate in a general way the optimum for an enzyme for the natural conditions under which it works. The alleged temperature optima are probably illusions: chemical reactions, whether they are catalysed by enzymes or not, are hastened by rise of temperature, but at the same time enzymes are progressively destroyed. The apparent optimum is simply the point at which the destruction of the enzyme just outweighs the increase in the rate of the reaction for purely

physical reasons, and will be higher the shorter the time for which the high temperature is allowed to continue.

1.31. Digestion in the Mammal, especially Man

The process of digestion follows a generally similar course in all vertebrates: our knowledge of the details is largely obtained from experiments on dogs, confirmed by clinical observations on man. The whole of the process goes on in the alimentary canal, the parts concerned being as follows.

The saliva in the mouth is produced partly by small buccal glands, but chiefly by three or four pairs of salivary glands—the submaxillary, the sublingual, the parotid or retrolingual, and the infraorbital. The last is absent from man but present in the dog and rabbit. In man about a litre of saliva is produced a day. It contains a protein called mucin, and its chief value is to act as a lubricant. It is secreted at pH 6.4–7.0, but it is said to go alkaline on standing through loss of carbon dioxide.

The gastric glands of the stomach are tubular and form gastric juice: this contains, besides mucus and enzymes, 0.2–0.6 per cent. of free hydrochloric acid, sufficient to give a pH of 1 even in the presence of proteins, which act as buffers. (Tenth Normal acid is about 0.4 per cent.) This acid is a disinfectant, though not all Bacteria are killed by it. Enzymes, mucus, and acid are secreted by different types of cell.

The secreted contents of the intestine come from four sources. Brunner's glands, at the upper end only of the duodenum, produce mucus, the function of which is to protect the epithelium from the acid of the stomach. Succus entericus, the intestinal juice proper, is produced mainly by tubular glands in the Lieberkuhn's follicles (the crypts between the villi) of the duodenum. The pancreas produces pancreatic juice. The liver produces bile,

which contains no enzymes, but which is nevertheless of great importance in digestion. After secretion it is in most mammals, including man, stored in the gall-bladder, where water is absorbed until the solids are ten times as concentrated as they were on arrival. The bile contains sodium chloride and bicarbonate, the pigments bilirubin and biliverdin (which are break-down products of haemoglobin), lecithin and cholesterol, and the characteristic bile salts. These vary in different animals, but are always salts of acids closely related to cholesterol. In man the chief are sodium taurocholate and sodium glycocholate.

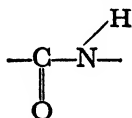
The secretions of Brunner's glands and the pancreas are alkaline, the bile is nearly neutral, and the succus entericus has a pH of 6.0. Although the pH of the pancreatic juice is not above 8.9 it represents about N/10 base, since the alkalinity is caused by bicarbonate, which acts as a powerful buffer. The acidity of the food passing into the intestine from the stomach is partially neutralized, but actual alkalinity is probably never reached. The pH of the duodenal contents is 4.5-5.1, that of the ileal contents 6.0-6.5.

1.311. Digestion of Proteins

There is no digestion of protein in the mouth. In the stomach the acid breaks up the collagen which forms the white fibres of connective tissue, and so liberates the individual cells, which are then more readily acted on by the enzymes. The elastin of elastic fibres is indigestible. The chief enzyme is a proteinase called pepsin, which has a pH optimum of 2 and hydrolyses proteins to proteoses and peptones, both of which are soluble. Protoplasmic cell walls are therefore broken down, and their contents liberated. The droplets of fat from the food give a milky appearance to the stomach content, which is then called chyme. Caseinogen, the protein of milk, is changed by

rennin to casein, and this is precipitated as the calcium salt, so that the milk clots. The acid of the gastric juice brings the casein into solution again as the hydrochloride.

The pancreas produces trypsinogen, which combines with enterokinase in the succus entericus to form trypsin. This is a mixture of enzymes: tryptic proteinase breaks proteins down to proteoses, peptones, and polypeptides, and then carboxypolypeptidase splits the polypeptides to dipeptides and a few aminoacids. In addition, the pancreas produces a protaminase, which does not need to be activated by enterokinase, and which hydrolyses protamines to polypeptides and aminoacids. A polypeptide is a substance which contains several of the peptide



linkages which are characteristic of the protein molecule; a dipeptide contains only one of these. Trypsin is incapable of breaking down the polypeptides entirely to aminoacids. Its optimum pH *in vitro*, that is, in glass vessels in the laboratory, is 8.0-9.7, but it is very unstable in this range. Trypsinogen by itself is capable of hydrolysing some simple proteins such as peptones; the reaction by which it forms trypsin is not an enzyme one.

The succus entericus contains erepsin, which has an optimum pH of 7.8. It consists of an aminopolypeptidase which acts on polypeptides, giving dipeptides and aminoacids, and a dipeptidase which splits dipeptides to aminoacids. The difference between the names of this polypeptidase and of the one present in trypsin indicates the different parts of the molecule of the substrate which they attack. The dipeptidase works on the amino group. Intestinal juice contains a little tryptic enzyme, and pancreatic juice some erepsin, but both are in small quantities only.

The total result of the action of all these enzymes is to break proteins down to their constituent aminoacids.

There are substances in nuclei which are called nucleoproteins; in them an ordinary protein molecule is combined with nuclein, which in its turn consists of a protein part combined with nucleic acid. This is made up of four mononucleotides, each consisting of a carbohydrate, phosphoric acid, and a base. In animal tissues the carbohydrate is usually *d*-ribose, which has five carbon atoms, and the bases are ring compounds, two purines and two pyrimidines. Nucleoproteins are first attacked by pepsin, which removes part of the protein portion of the molecule, leaving nuclein. Trypsin removes the rest of the protein part, and so liberates nucleic acid. The duodenum contains a number of enzymes which deal with this: polynucleotidase splits it into its constituent mononucleotides, from these nucleotidase separates phosphoric acid, and finally nucleosidase separates the carbohydrate and basic parts of the molecule. It is likely that part at least of these last three reactions takes place in the cells of the mucosa.

1.312. Digestion of Fat

Fat is liberated in the stomach when the nitrogenous cell walls are dissolved, and the acid, a lipase in the gastric juice, and regurgitated lipase from the duodenum, start hydrolysis, chiefly of finely divided fat such as that of egg-yolk. In the intestine there are lipases (optimum pH 8.0) from the pancreas and the succus entericus, and their action is greatly helped by the presence of bile. The bile salts lower surface tension, so breaking up the droplets of fat to a finer emulsion, but further they are hydrotropic, that is they can bring other substances, including fats, fatty acids, and calcium soaps, into true solution. In this they are greatly assisted by the lecithin in the bile. In men without bile, 65-70 per cent. of ingested fats are

absorbed, so that this secretion is helpful rather than essential in digestion. Lipase hydrolyses fats to fatty acids and glycerol. Since the intestinal contents are never alkaline, soaps cannot be formed.

1.313. Digestion of Carbohydrates

The saliva of most mammals is free, or nearly free, from enzymes, but that of Primates, pigs, and some rodents contains an amylase called ptyalin (optimum pH 6.5) which breaks down starch to maltose and a series of dextrans. The reaction is:

starch → soluble starch

→ erythroextrin → achrooextrin → stable extrin
 + maltose + maltose + maltose

Erythroextrin is so called because it gives a red colour with iodine. Ptyalin requires the presence of a small quantity of salts, particularly sodium chloride, for its action. The extent to which salivary digestion goes on depends on the time during which the food remains in the mouth. When the swallowed food is made strongly acid in the stomach the action of ptyalin is stopped, but the acid takes some time to diffuse into solid food, and it may be as long as forty minutes before hydrolysis ceases. By this time very little starch is left. The amylase of animals, whether it is formed in the salivary glands or the pancreas, is quite incapable of attacking raw starch grains. These must first be broken down, either in the preparation of the food as by boiling, by chewing, by Bacteria, or by enzymes contained in the food itself. Amylase can also hydrolyse glycogen to maltose, and the saliva contains a small quantity of maltase.

The gastric juice itself contains no enzymes which act on carbohydrate, but the duodenal contents regurgitate into the stomach. The acid hydrolyses cane sugar, and also

inulin, which, since it is the normal storage compound of the Compositae, will occasionally occur in the food of man in such things as the Jerusalem artichoke and salsify. Since vertebrates have no inulase, the action of the acid is the only way in which inulin can be digested.

The small intestine contains an amylase and a maltase from the pancreas, and a sucrase, a maltase, and a lactase from the succus entericus. The amylase has a pH optimum of 7.0, and acts just like ptyalin, with which it may be identical. The other enzymes, which are called collectively hexosidases, hydrolyse the appropriate disaccharides to monosaccharides; maltase splits maltose to two molecules of glucose, sucrase splits sucrose to glucose and fructose, and lactase splits lactose (milk sugar) to glucose and galactose. Lactase is especially prominent in young mammals.

Cellulose is very resistant; lignocelluloses are seldom digested, and the simpler types can only be attacked by special enzymes called cellulase and hemicellulase, which are not formed by vertebrates. The cellulose cell walls in the food of herbivorous mammals are dissolved partly by autolysis of the dead cells by their own enzymes, and partly by the action of symbiotic Bacteria. These are very prominent in the caecum of the rabbit and the rumen of artiodactyls. In these, the animals which chew the cud, food is swallowed without being chewed, and passed into a complicated 'stomach' (Fig. 4). The part of this which contains gastric glands and corresponds to the stomach of other mammals is the last chamber or abomasum. After being swallowed the food is circulated through the rumen and reticulum, where the cellulose is attacked by Bacteria. The food is regurgitated into the mouth and chewed, and then swallowed a second time. It undergoes further mechanical trituration by the folds of the psalterium, and then goes to the abomasum for normal digestion. In connexion with

the long time taken to digest cellulose, it is significant that herbivores have a much longer gut than carnivores of similar size.

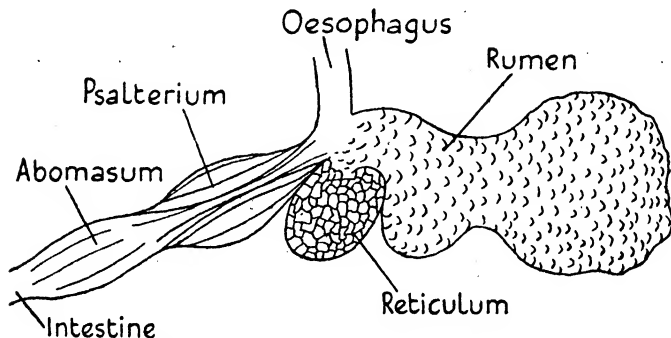


FIG. 4. Stomach of sheep, cut open, semi-diagrammatic.

1.314. Absorption

There is practically no absorption of water or solutes in the stomach. In the intestine the surface is greatly increased by the villi, which have a characteristic structure (Fig. 5), and it is into these that the digested food goes. Water, salts, hexoses, pentoses, and aminoacids pass into the blood capillaries, but the mechanism by which they do so is unexplained. An animal's own blood serum can be absorbed, and a dog's intestine can take up a solution of common salt which has an osmotic pressure twice that of the blood. This cannot be simple osmosis, but even with a dead membrane, if it has differential permeability to a number of solutes which are present, water and solutes may travel in what is apparently the wrong direction. Moreover, the cells may be capable of doing work against the osmotic pressure. Hexose is absorbed in combination with phosphate; disaccharides, despite their diffusibility, are not absorbed at all.

The fatty acids, brought into solution by the bile salts,

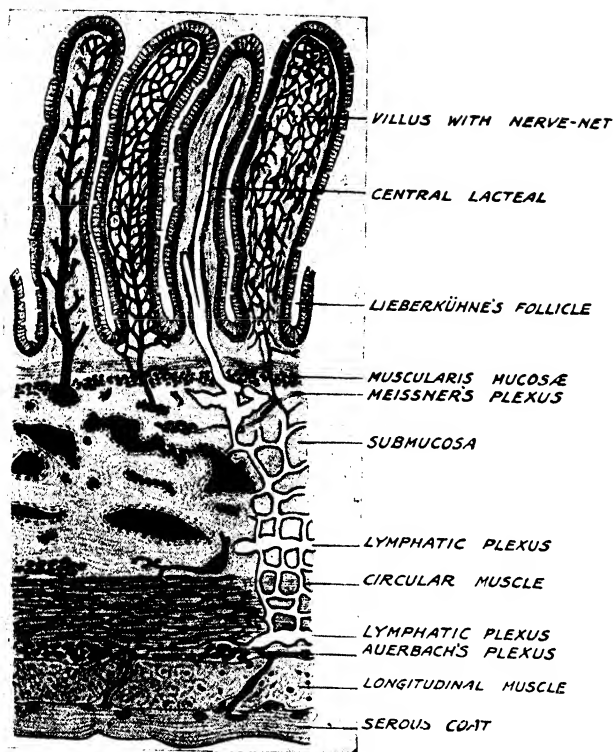


FIG. 5. Diagrammatic section through wall of small intestine to show vascular and lymphatic arrangements. After Schaffer.

are absorbed by the epithelial cells of the villi; phosphatase is necessary for this to go on. A certain amount of resynthesis to neutral fat takes place, and this and unchanged fatty acid are passed somehow into the reticular tissue of the villus, and from there into the lumen of the central lacteal. Different acids are absorbed at different rates, and so the neutral fat in the lymph does not have the same composition as that in food. Moreover, some of it is present as phosphatide, which has presumably been formed during absorption under the action of the phosphatase. A phosphatide is a complex ester of glycerol with aliphatic acids and phosphoric acid, often containing a nitrogenous basic group as well. The villi undergo a constant pumping action, which helps to empty the lacteals into the plexus of lymphatics with which they connect. The milky liquid in the lacteals is called chyle. The lymphatics finally open into the left jugular vein by the thoracic duct, so that the fat goes into the general circulation.

In the small intestine practically all the food becomes dissolved. The material passed into the colon consists mainly of mucus, dead Bacteria, and excretions such as bile and salts of heavy metals. Only when the food contains a large amount of indigestible cellulose is any appreciable part of it present. Some water is absorbed, and the remains are ejected through the anus as faeces.

Food has generally passed through mouth, stomach, and small intestine in four and a half hours. The stay of any residue in the colon is much longer, up to three or four days or more.

1.315. The Movement of the Food

In man and many other mammals the food in the mouth is masticated, that is to say it is broken up by the cheek teeth and rolled into a bolus by the tongue. The degree

of chewing which is possible depends on the jaw articulation and this on the food. In Carnivora the dentary has a hinge-like joint with the squamosal, and lateral movement of the jaw is impossible: there is no chewing. In Artiodactyla the glenoid surface is flat, and the dentary can be moved widely from side to side so that the cellulose walls of the food can be broken up. Man, omnivorous, is intermediate between these two. Mastication is voluntary, but it may be reflex, each closure of the jaws acting as a stimulus for their reopening. After chewing, the bolus is swallowed: deglutition or swallowing starts as a voluntary movement, but its accomplishment is a chain of reflexes involving the movement of the food by peristalsis, the closure of the nasal and tracheal openings, and the cessation of breathing. Cranial nerves V, IX, X, and XII are involved. Peristalsis is the muscular contraction characteristic of the gut, and depends on the fact that if the gut is stimulated at any point, as by the presence in it of food, the muscles contract so as to hold back any material which is above, and to push on that which is below. The old Law of the Intestine, according to which the muscles contract immediately above a stimulus and are inhibited below, is not strictly true, though it sometimes holds for circular muscle. Antiperistalsis, which sometimes occurs by a local reversal of the reflex, moves the food in the opposite direction. If the food is fluid it enters the stomach six seconds after the beginning of the act, but if it is solid it takes much longer, up to fifteen minutes, to pass down the oesophagus.

In the stomach the food is thoroughly mixed by a series of waves of contraction, three or four a minute, which pass from the middle of the stomach to the pylorus. These tend to drive the food in the same direction, but since the pylorus is closed there is axial reflux, giving very good mixing. This peristaltic contraction, which starts on the entry of food, is myogenic, that is to say its co-ordination

is independent of any nerve supply. After a time—about a minute when water has been swallowed—the pylorus relaxes at each wave, allowing some of the stomach contents to enter the duodenum. The mechanism by which the pylorus is controlled is not clear, but the central nervous system seems to be involved. Fat stays in the stomach

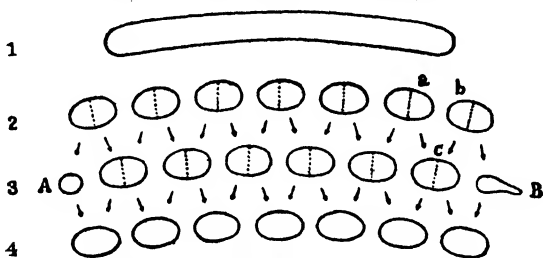


FIG. 6. Diagram of the 'segmentation' movements of the intestines as observed by Röntgen rays, after administration of bismuth.

1. A continuous column, intestinal movements being absent.
 2. The column broken up into segments.
 3. Five seconds later, each segment divided into two, the halves joining the corresponding halves of adjacent segments.
 4. Condition (2) repeated five seconds later.
- After Cannon.

longer than carbohydrate, but all food has generally left in three or four hours. Vomiting is caused by compression of the stomach by a violent contraction of the diaphragm. Antiperistalsis is normal in the stomach and oesophagus of artiodactyls, so that food is returned to the mouth.

In the small intestine the food continues to be moved by peristalsis, controlled by the deep nerve plexus (Auerbach's). In the duodenum there is some antiperistalsis, so that food can be regurgitated into the stomach, particularly when that viscus is empty. The small intestine also undergoes segmentation movements, by which the food contents are thoroughly mixed. The wall becomes constricted into a number of segments, and then about five seconds later the constrictions disappear and are replaced by another set exactly out of phase with the first (Fig. 6).

The large intestine undergoes infrequent powerful contractions, particularly when food is taken. The normal stimulus for defaecation is the filling of the rectum, and it is carried out by contraction of this viscus, aided by that of the voluntary abdominal muscles.

1.316. The Co-ordination of Secretion

There is a complicated and varied mechanism for ensuring that the digestive juices are available when they are wanted. Saliva is secreted as the result of taste stimuli picked up in the mouth by the fifth and ninth cranial nerves. The glands are stimulated by parasympathetic fibres in V, VII, and IX, and by the cervical sympathetic. As a result of the formation of conditioned reflexes (see section 6.4) saliva may be formed on the receipt of any stimulus, such as a dinner gong, connected with meals, or even by an advertisement or the mere thought of food. Gastric secretion is started by meat in the mouth through a similar appetite reflex, which also may become conditioned to new stimuli, and is continued in two other ways. Peptones in the stomach cause the pyloric mucosa to produce a hormone, gastrin, which circulates in the blood and stimulates the gastric glands, and food in the duodenum causes the production of another hormone which acts similarly. The gastric juice from the reflex varies in quantity with the appetite, but is constant in composition, while that produced by the hormones varies in quantity and quality. The largest volume is produced after meat, but the greatest digestive power after bread.

The secretion of succus entericus is mainly due to local mechanical stimulation of the mucosa, Meissner's plexus apparently being involved, but there is some chemical stimulation as well. The pancreas is stimulated to produce enzymes by the vagus, but a hormone called secretin, produced by the intestinal mucosa when acid comes in

contact with it, causes the secretion of bicarbonate. The neutralization of the stomach contents is therefore under exact control, for the acid acts as a stimulus for the production of alkali, and when the intestinal contents are nearly neutral no more secretin, and so no more bicarbonate, are produced.

Bile is at least in part an excretion, and its production is naturally continuous. It is, however, increased by the presence in the intestine of protein, fat, bile salts, or dilute acid, or by the presence of secretin in the veins, so that more of it is formed when it is wanted. The gall-bladder, which is innervated by the vagus, is stimulated to contract by the sight of food or the act of eating, and by a hormone called cholecystokin, formed by the duodenal mucosa, when it comes in contact with food, particularly fat and egg-yolk. Both these are substances which need bile salts for their digestion.

1.32. Digestion in Other Vertebrates

The general course of digestion seems to follow the same lines in other vertebrates as in mammals. Salivary digestion is rare, but the stomach secretes a pepsin-like enzyme acting in acid medium, the intestinal proteases are distributed as they are in mammals, and the intestine contains amylase, hexosidases, and lipase. In bony fishes, however, both amylase and maltase are secreted predominantly by the pancreas. Little work has as yet been done on the identity of the enzymes in the different classes, but the individual proteases are certainly very similar, if not identical, in fish, Amphibia, reptiles, and mammals.

1.33. Digestion in Invertebrates

Until comparatively recently the only method available for investigating the presence of enzymes in invertebrates was to make an extract of the gut or of a gland, and

observe its effect on various substrates *in vitro*. This has been done for most of the phyla, and it has been found that nearly all animals possess, in greater or less degree, proteases, carbohydrases, and lipases, only a few groups being lacking in one or other of the last two. Since the food of animals consists of proteins, carbohydrates, and fats, and of little else, these results merely give us proof of what might with little risk have been assumed *a priori*. The methods of extraction which have been used have often been rather crude, and it is often by no means certain that the enzymes identified are really secreted into the gut in the sense of being passed outside the cells. The more recent and valuable work on enzymes has involved careful preparation of the extract, exact quantitative following by analytical methods of the change of the substrate to its scission products, and meticulous attention to the hydrogen-ion concentration and other physical properties of the medium. Recently Willstätter and Waldschmidt-Leitz have introduced adsorption methods which enable enzymes to be separated from one another. This has for the first time made it possible to compare the enzymes of different animals. In the light of this last method of attack the earlier work, on the mere occurrence of the three great groups of enzymes, is of little interest. Beyond showing that enzymes were present, the only result of importance which it gave was the observation that the relative concentration of the enzymes in the gut bore a general relation to the type of food. For example, the closely related flies *Glossina* and *Calliphora* both contain protease, carbohydrase, and lipase, but while the blood-sucking *Glossina* has much protease and little of the other two, conditions in the vegetable-feeding *Calliphora* are exactly the reverse.

Careful adsorption methods, similar to those used to separate the proteases of vertebrates, have been applied

to only a few other animals. In the crab *Maia squinado* and in the marine snail *Murex anguliferus* it has been found that the gut contains the same four proteases as are present in vertebrates, namely proteinase, carboxypolypeptidase, aminopolypeptidase, and dipeptidase. Moreover the pH optima are of the same order as those for the vertebrate enzymes. Since the exact values of these optima depend on the degree of purification, exact equality is hardly likely to be obtained, but the similarity is sufficiently great for it to be probable that the proteases of these two animals are similar to, if not identical with, the vertebrate trypsin-crepsin group. The *Maia* proteinase does not need activation, but after it has been purified it becomes inactive, and can be reactivated by enterokinase. This suggests that the proteinase of *Maia* and of vertebrates is similar or identical, but that in the crab it is secreted along with its activator, which is separated in the purification by adsorption. Preliminary experiments on *Helix pomatia*, on the cuttlefish *Sepia officinalis*, on *Periplaneta*, and on a coral, have shown that in all these the protease consists of several components. For *Sepia* the pH optima are about the level of those for trypsin, and the proteinase requires activation by an extract of the caecum of the animal. This extract can be replaced by enterokinase, and can itself activate vertebrate trypsin: there is therefore little doubt of its identity with enterokinase. The general conclusion which may be drawn from all these results is that certainly in the Mollusca and Crustacea, and probably in the insects and coelenterates, protein digestion is carried out by the same series of four enzymes which are present in the intestine of vertebrates, and that it is at least possible that the four enzymes are identical in all these classes.

Invertebrates possess nothing which corresponds to pepsin.

An interesting case is that of the clothes-moth *Tineola*

biselliella, which lives largely on keratin and related compounds, which are not in the ordinary way attacked by enzymes. The pH of the gut is 10, and under these conditions the keratin is reduced by some system present in the gut to products on which the animal's proteinase can act. This proteinase cannot act on proteins *in vitro*, but it does act on keratin which has been attacked by a weak reducing agent.

The carbohydrases of invertebrates have not been so fully investigated as the proteases, but something has been made out as to their nature and distribution. Amylase from a number of groups has been shown to be very similar to vertebrate amylase: it hydrolyses starch to maltose, but cannot attack pure starch grains, and usually has a pH optimum slightly on the acid side of neutrality. In the oyster activation by salts is necessary, just as with ptyalin. In most cases it has not been separated from its associated maltase, but in the oyster they occur separately.

Inulase is present in the snail and some other animals. Cellulase and hemicellulase have been found in a number of invertebrates, notably the earthworm, the snail, the boring bivalve *Teredo*, some insects, and possibly the crayfish. There is some evidence that in the snail cellulase and hemicellulase are identical, but that the enzyme consists of more than one component, a true cellulase breaking the cellulose to an intermediate sugar, and another hydrolysing this to glucose. A few animals, such as the snail and some insects, possess chitinase. In *Helix pomatia*, where it is rather weak, it breaks chitin down to N-acetylglucosamine.

The three common hexosidases—sucrase, maltase, and lactase—have been found very widely in invertebrates, but next to nothing seems to be known about their relations with each other or with the vertebrate enzymes. In some animals many more sugars than sucrose, lactose, and mal-

tose can be hydrolysed, so that either several hexosidases are present or else one enzyme can act on more than one substrate. The snail in particular can digest a very full list of sugars and related substances—at least seventeen. As there is only a limited number of hexoses from which the other sugars are built up, the second explanation is quite probable.

Lipases as a group are much less specific than proteases and carbohydrases, and all glycerol esters seem to be hydrolysed to some degree by any enzyme of this class. Invertebrate lipases differ in a number of points from those of vertebrates; they are differently affected by ions, they are inhibited in different ways, and they differ in the ease with which they attack different substrates. In many cases the enzyme attacks esters of lower fatty acids more readily than oils or fats, so that it is more properly called an esterase than a lipase. The distinction, however, is a very fine one, and it seems that even in the same species sometimes the action is stronger on fats, sometimes on esters.

In the vertebrates, the different constituents of the enzymes acting on proteins and carbohydrates are very largely produced by different glands, and to some extent act in different parts of the alimentary canal. It was therefore easy to recognize that more than one enzyme of each sort was present, even before the modern work on separating them by adsorption was begun. On the other hand all the enzymes of an invertebrate are often produced by a single gland, and they nearly always act together in one part of the alimentary canal. This, while it means that the recognition of separate entities is difficult, also means that anatomically the gut of invertebrates is relatively simple. About such specialization as there is it is very difficult to generalize, so that each of the major groups must be taken separately. It can, however, be said that

intracellular digestion is primitive, and as such is the normal method in the coelenterates and Turbellaria. It has also been retained in some higher animals which feed in such a manner as to make it possible. Of these the chief are the lamellibranchs and lower gastropods, which feed on minute vegetable particles, and the arachnids, which break down the food externally to fluid and small particles which can easily be absorbed by the cells. In many echinoderms and lamellibranchs there is a special form of intracellular digestion; large food particles may be taken up and ingested by wandering amoebocytes, which in lamellibranchs may even go outside the animal and ingest food in the mantle cavity. They can attack all three classes of food and are probably of some importance.

The advantages of extracellular digestion are many. It reduces the internal area of the gut necessary for absorption, it hastens digestion and the voiding of indigestible matter, and it enables the enzyme-secreting glands to become specialized. The last process has only just begun in invertebrates, but as described above it is well developed in the vertebrates.

In the Protozoa digestion goes on in vacuoles. In all the genera which have been investigated by modern methods it has been found that the vacuoles rapidly become acid (they reach a pH of 4.0 in *Paramecium*) and that digestion goes on under these conditions. The acidity may be due at least in part to the cytolysis of the food, as the prey is always killed before there is any great departure from neutrality. When digestion is finished the hydrogen-ion concentration gradually returns to normal, and defaecation occurs somewhere between pH 5.0 and 7.0. Protozoa seem to find proteins the easiest food to digest, many having difficulty with carbohydrate and fat. *Amoeba proteus* digests fat to glycerol and fatty acids, which pass into the cytoplasm and are there resynthesized, but *A. dubia*

takes some days to digest olive-oil and *Typanosoma evansi* seems to contain neither lipase nor carbohydrase.

An account of protozoan digestion would be incomplete without a reference to the fact that the green flagellates are photosynthetic and sometimes (e.g. *Euglena*) saprophytic as well. Photosynthesis is, however, typically a phyto-logical phenomenon, and it would be out of place to discuss it here.

In the coelenterates there are no special digestive glands, but in the Scyphozoa the glandular cells are concentrated on the gastric filaments and in the Anthozoa on the mesenterial filaments. The enteron contains a proteinase which starts the hydrolysis of proteins. The further break-down of these, and the entire digestion of fats and carbohydrates, are intracellular. Before the food particles are absorbed they may be moved about by peristalsis or ciliary currents or both. Indigestible parts of the food are extruded by the mouth, and may be removed by the ciliary currents. The green Algae which live symbiotically with many corals are of no help in supplying food.

Most of the Turbellaria which have been examined resemble the coelenterates in that only the preliminary break-down of proteins is extracellular. In some of the Rhabdocoelida, however, digestion is mainly or perhaps entirely extracellular. The pharyngeal glands of the Turbellaria secrete mucus, and in some species of Rhabdocoelida their secretion contains enzymes which are used for external digestion.

The pharynx of the earthworms contains a proteolytic enzyme, but apparently no others, so that it is possible that it comes from the pharyngeal (salivary) glands, which are otherwise merely mucus-producing. In the intestine, digestion of all types of food takes place, and in general, secretion seems to be carried out by the gut wall.

The Lamellibranchia are peculiar amongst relatively advanced animals in that most of their digestion is intracellular. The only enzyme set free in the gut is the amylase formed in the crystalline style. The latter is a rod of

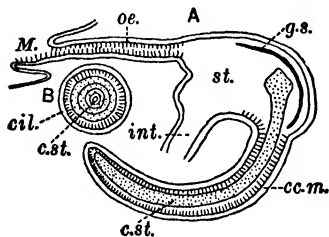


FIG. 7. Sections of part of the alimentary canal of *Donax*.

A. Longitudinal section, showing *cc.m.*, caecum of the intestine containing *c.st.*, crystalline style; *g.s.*, gastric shield; *int.*, intestine; *M.*, mouth; *oe.*, oesophagus; *st.*, stomach. B. Transverse section across the caecum showing *cil.*, ciliated epithelium, and *c.st.*, crystalline style composed of concentric layers of material. After Barrois.

of globulin (a protein), but containing food particles and the enzyme as well (Fig. 7). It is secreted in a style sac in the intestine, and is rotated by means of cilia, its speed in the young oyster being about 70 r.p.m. It is gradually worn down in front so that the amylase is liberated and at the same time brought into very close contact with the food. The function of the protein is to maintain the pH of the gut at about 5.5, which is optimal for the amylase. In many genera the stomach has a special filtering mechanism which allows only small particles to pass into the digestive diverticula, in the cells of which further digestion takes place. Muscle is almost entirely absent from the gut, so that all the movement of the food is by cilia, which maintain a circulation through the diverticula. The more primitive Gastropoda closely resemble the lamellibranchs in their methods of digestion. Some, such as *Crepidula*, possess a style, and this produces the only extracellular enzyme, which is an amylase. In *Patella* and other genera which are without a style the amylase, again the only extracellular enzyme, is produced by lateral diverticula of the foregut. In carnivorous forms, like *Murex*, there are extracellular proteases, which may be formed by the digestive diverticula or by buccal glands or

both. In the Pulmonata, such as *Helix*, most of the digestion is extracellular, but peptides must be absorbed before they are broken down to aminoacids. In all gastropods most of the digestion, as well as absorption, takes place in the digestive diverticula. The radula is an important feeding organ, and is lubricated by the secretion of the buccal glands. In *Dolium* and *Murex* these also produce the sulphuric acid for the solution of the calcareous shells of the bivalves on which these animals feed.

There is no intracellular digestion in the Crustacea, and all the movement of the food is by muscles, since cilia are entirely absent from the group. In the decapods the food is well broken up in the gastric mill, and is at the same time attacked by a protease which is sent forward from the digestive diverticula. At the entrance to the latter there is a complicated filter which allows only fine particles to pass. All the further digestion and most of the absorption take place here, the main midgut region being extremely short. Material is taken into the diverticula by the contraction of longitudinal muscles, and expelled by the contraction of circular muscles.

In some insects the labial glands contain an enzyme, for instance amylase in the cockroach, and in any case they usually form a liquid which softens the food. Glands seldom open into the crop, but digestion may take place

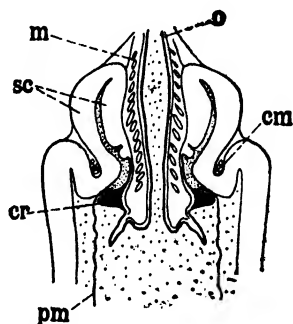


FIG. 8. Diagram of gut of earwig, *Forficula*. After Wigglesworth. The peritrophic membrane is squeezed out as a tube surrounding the food by a press formed from the posterior part of the foregut.

cr., circular ring forming inner wall of press; *cm.*, circular muscle compressing the outer wall against this ring; *m.*, sphincter muscle; *o.*, oesophagus; *pm.*, peritrophic membrane; *sc.*, cells secreting the substance of the membrane.

here by enzymes sent forward from the midgut, as for example in the cockroach, where fat is digested and absorbed in this region. In this animal and many others most of the crop digestion is carried out by yeasts and Bacteria, which are subsequently themselves digested by their host. Midgut digestion is by enzymes in the normal way. When an insect is feeding on solid food, the bolus on leaving the foregut is enclosed in a thin sac of chitin called the peritrophic membrane (Fig. 8). This is permeable to both enzymes and digested food, and absorption takes place through it. The chief function of the hindgut is to absorb water, loss of which is very dangerous to insects, but in some beetle larvae digestion of symbionts and absorption of the products takes place.

1.4. Intermediate Metabolism

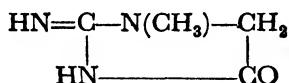
All the soluble materials which the blood obtains from the small intestine suffer one of two fates: they may be built up into the tissues of the body, or they may be broken down to supply energy. In either case they undergo complex chemical changes of which relatively little is known. It will be convenient to deal with the three classes of foodstuffs separately.

1.41. Protein Metabolism

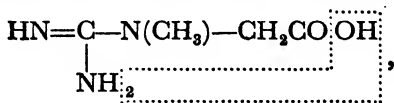
The aminoacids derived from the proteins of the food are the animal's chief source of nitrogen, and there is no doubt that they are the materials from which protein is built up. The chemistry of the process is, however, obscure. There is no doubt that enzymes which can split proteins could, under appropriate conditions, catalyse the reverse reaction, but there is no evidence that this is what goes on in the body. It is at least possible that aminoacids might be further broken down, and the resulting substances built up directly to proteins. Not all the aminoacids are necessary for life or even for growth, and some at least

of them can be synthesized. The reaction apparently takes place between ammonia and keto- or hydroxyacids. Since the latter (e.g. lactic acid) can be formed from carbohydrate, it is possible that some of the protein substance of the body is derived in part from carbohydrate. Nevertheless, proteins are an essential part of the food, and since most of the aminoacids certainly cannot be synthesized in sufficient quantity, those proteins which give them on hydrolysis are necessary in the diet.

If human urine is analysed after the subject has been living on a diet rich in protein, and again after a diet with minimal quantities only, it is found that whereas the amount of urea excreted is much greater in the first case, the amount of creatinine is practically the same in both. This suggests that the formation of the latter substance is not immediately dependent on protein in the food, and that it is in fact derived from tissue break-down. Nitrogen derived from this source is called endogenous. Creatinine has the formula



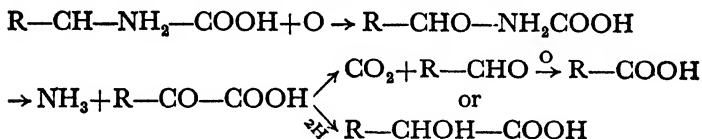
and is probably derived by dehydration from creatine,



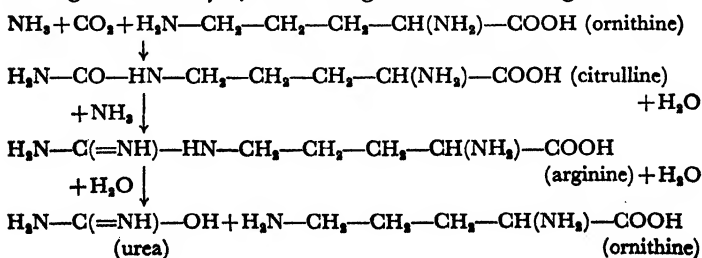
which is important in the contraction of voluntary muscle (see pp. 87-93). The mode of origin of creatine from proteins is unknown.

In the adult mammal there is practically no growth, so that except in the pregnant female very small amounts of nitrogen are needed for repair and the manufacture of enzymes and other secretions. The rest of the nitrogen in the food is split off from the aminoacids in exogenous

metabolism. There is no doubt that in mammals most of it is excreted in the urine as urea. The process by which the nitrogenous part of the aminoacid molecule is separated from the rest is called deamination, and it goes on in the liver and in some other tissues, such as kidney, as well. The chemistry of the process has been investigated by feeding animals with aromatic aminoacids. The intermediate products formed from aliphatic acids have only a transitory existence, but since the benzene ring is not easily oxidized in the body, similar substances formed from aromatic compounds appear in the urine. It seems that α -aminoacids undergo oxidation at the α -carbon atom and split off ammonia. The ketoacid thus produced may be then oxidized to a fatty acid or reduced to a hydroxyacid.



In this process there is very little heat change, and the fatty acids produced still have about 95 per cent. of the available energy of the original aminoacid. The residues of some aminoacids can be changed to glucose in the liver. Some of the ammonia combines with acids and is excreted as ammonium salts, but most of it reacts with carbon dioxide to form urea, the aminoacid ornithine acting as a catalyst, according to the following scheme:

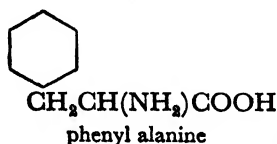
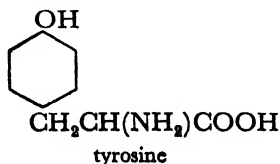


The last reaction, the hydrolysis of arginine, is carried out by the enzyme arginase. The same cycle has been shown to operate in the livers of fishes and of the frog and the tortoise (*Testudo graeca*). It does not occur in birds; and in mammals also other mechanisms exist.

Birds, and the Squamata (lizards and snakes) excrete most of their nitrogen not as urea but as uric acid. How the latter is formed by the deamination of proteins is unknown, but it is certain that in birds neither urea nor arginine is involved in its production, but that probably hypoxanthine is. The basic compounds from which it is manufactured are ammonia and lactic acid. Birds do produce a little urea, probably by the action of the little arginase which they possess on arginine directly derived from proteins in the food.

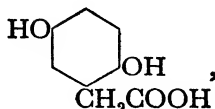
The vertebrates can therefore be divided into two main groups: the mammals, Chelonia, Amphibia, and elasmobranchs, which excrete exogenous nitrogen chiefly as urea and are called ureotelic; and the birds and Squamata, which form uric acid and are called uricotelic. The significance of this division is discussed in section 8.2. The teleosts and Crocodilia form a third division; the latter excrete their nitrogen directly as ammonia, and the former as ammonia and trimethylamine oxide.

As has been said, the body does not usually oxidize the benzene nucleus, but it is able to deal with the three known aromatic aminoacids,



and tryptophane (formula p. 2). These are normally completely oxidized, but in the hereditary disease alkaptonuria,

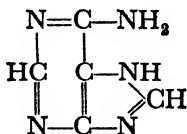
tyrosine and phenyl alanine are converted to homogentisic acid,



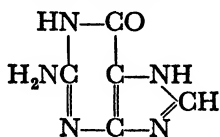
which is excreted in the urine. When this is allowed to stand the acid is oxidized to dark pigments giving the sign which is characteristic of the disease.

At some stage in the break-down of proteins the sulphur which they contain is separated as sulphate, which is excreted in the urine. Endogenous sulphur appears in the urine in various forms, such as thiocyanate and mercaptans, which are called collectively neutral sulphur.

The purines derived from nucleo-proteins in the food may, like aminoacids, either be built up into constituents of the body or broken down immediately. In the former case there is later some destruction by endogenous metabolism. Adenylic acid, for instance, which is important in muscular contraction, gives uric acid. This substance is also produced in exogenous metabolism. On digestion of nucleic acid, adenine (6-amino-purine)

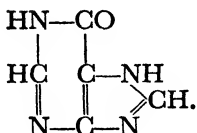


and guanine (2-amino-6-oxypurine)

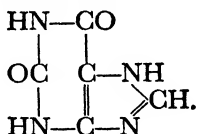


are formed. The first of these then loses ammonia in

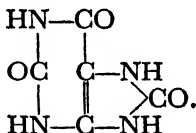
deamination by the enzyme adenase to hypoxanthine (6-oxypurine)



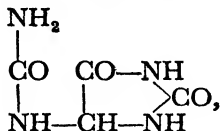
The second is similarly hydrolysed by guanase to give ammonia and xanthine (2-6-dioxypurine)



Hypoxanthine is oxidized to xanthine, and this under the influence of the enzyme xanthine oxidase then gives uric acid (2-6-8-trioxypurine)



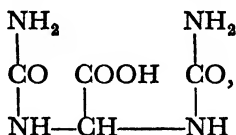
In most mammals a further enzyme, uricase, is present, which acts on the uric acid giving allantoin,



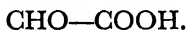
in which the purine ring has been broken. Uricase is absent from man, the higher primates, and the Dalmatian dog, so that these animals excrete uric acid and are liable to suffer from gout.

The uricotelic vertebrates do not possess uricase, so in them uric acid is the end-point at which nitrogen arrives

whether it starts by being part of a protein or of a nucleoprotein. In the Amphibia and fishes uricase is present, and there are in addition allantoinase, which breaks the purine ring again and hydrolyses allantoin to allantoic acid,



and allantoicase, which hydrolyses this substance to two molecules of urea and one of glyoxylic acid,



In these forms, then, the nitrogen from nucleoproteins is excreted as urea.

Little is known of intermediate nitrogen metabolism in invertebrates, but it appears that in annelids, decapod Crustacea, and molluscs it begins by a process similar to what occurs in vertebrates: ammonia is split off from aminoacids, and converted to the appropriate product to be excreted. The division into ureotelic and uricotelic groups probably applies to some extent, though many of the aquatic forms excrete their nitrogen directly as ammonia. The insects, like the birds, are uricotelic. Some silkworms are unable to digest starch, and are probably able to synthesize carbohydrate from protein. Maggots can use protein for making fat.

1.42. Fat Metabolism

Fatty acids enter into cell structure in two ways: they may be an essential constituent of protoplasm, where they are particularly important in the structure of membranes, or they may be present as formed materials which are easily removed and which are by no means essential for life. In the first case they are mostly combined with

phosphoric acid as phosphatides, while in the second case they are usually in the form of neutral triglycerides, the ordinary fat of common speech. Both forms are in part built up by the animal from the fatty acids absorbed by the small intestine. There is some general connexion between the fats in the protoplasm and those taken in the food, but each tissue of each species maintains its fats fairly constant in composition: there must therefore be some power to change one fatty acid to another. Some of the stored fat is formed from carbohydrate (see below).

Fat is burnt by the animal to supply energy, and normally the combustion is complete. In the disease diabetes mellitus, however, and in starvation, where excess of fat has to be used, abnormal products appear in the urine of mammals. Similar substances are formed if an animal is fed with fatty acids containing a phenyl group (cf. above, p. 38). It seems reasonable to suppose that these substances, which are ketones and β -hydroxy- and β -ketoacids, are intermediate products in fat katabolism. On this supposition the theory of the β -oxidation of fats is based. It is presumed that oxidation goes on at the β -carbon atom until the fatty acid with two carbon atoms fewer than the original one is produced. This in its turn is oxidized in the same way, and the process of losing carbon atoms two at a time goes on until aceto-acetic acid is produced, and this is finally oxidized to carbon dioxide and water. The appearance of the keto-substances in the urine on a diet lacking carbohydrate has led to the suggestion that they react with this before their final oxidation. There is, however, no certain evidence of this. The β -oxidation goes on in the liver, but the oxidation of the aceto-acetic acid elsewhere, possibly chiefly in the kidney. There are certainly other less important methods of fat oxidation, such as ω -oxidation, in which a carboxyl group

is introduced at the far end of the molecule from the one already present, and oxidation then goes on from both ends. It is possible, but by no means certain, that fats can be converted into carbohydrate.

Fat is commonly stored in the connective tissue of all vertebrates, though Amphibia have little of it. It is also found as a storage compound in many invertebrates, as in the Platyhelminthes, in the yellow cells of earthworms, in molluscs, and in the digestive diverticula and gonad of crustaceans.

1.43. Carbohydrate Metabolism

All the carbohydrate, other than the little which gives rise to pentoses, is changed in the gut into one or more of the hexoses glucose, fructose, and galactose. These three can very easily be changed one into the other, and there is no doubt that the animal can do this. The chief carbohydrate present in the blood is glucose, which is undoubtedly the normal sugar of transport. Carbohydrate in the mammal is stored as glycogen both in the liver and in the muscles, and there is a cycle connecting the two. Glucose is carried in the portal vein to the liver, and is there possibly built up to glycogen. The hepatic vein, however, normally contains more glucose than does the portal vein, even after a meal, and the liver is certainly breaking down glycogen more rapidly than it is building it up from glucose. The hydrolysis takes place chiefly by phosphorolysis. The glucose in the hepatic vein is carried to the muscles, and is there synthesized to muscle glycogen. This is broken down when the muscle contracts (see pp. 87-90), or by the action of adrenalin, to lactic acid. This is carried in the blood to the liver, where it is re-synthesized to glycogen. There is thus a circulation of carbohydrate. Frog's muscle can convert lactic acid to glycogen, but it is not known that mammalian muscle

can do so. In starvation or severe exercise the muscle glycogen is maintained at the expense of the liver glycogen. Glycolysis, the break-down of glucose to lactic acid, also occurs in the blood. By all these reactions the concentration of the blood-sugar is kept constant within fairly wide limits (80–200 mg. per 100 ml. in mammals). If the blood-sugar falls below the lower limit hypoglycaemia occurs, and after convulsions and fall of temperature death soon follows. Hyperglycaemia, excess of sugar in the blood, leads to excretion of glucose in the urine.

The hormone insulin, formed by the islets of Langerhans in the pancreas, is important in controlling the blood-sugar. It seems to act both by inhibiting glycogen break-down and accelerating glucose oxidation. It also retards formation of carbohydrate from aminoacids. It is liberated into the blood when carbohydrate is taken in the food, but how is not known. A deficiency of insulin causes the disease diabetes mellitus, in which glucose is excreted in large quantities in the urine. This can be treated only by administration of insulin, which must be carefully regulated to the amount of carbohydrate in the food, as otherwise either hyperglycaemia or hypoglycaemia will result. The anterior pituitary produces a hormone which is antagonistic to insulin; excess of it causes hyperglycaemia, as would be expected.

Some of the carbohydrate in the food is undoubtedly changed to fat. The chemistry of the process is complicated, and although several schemata are in existence they are all mainly hypothetical.

Glycogen is apparently one of the main storage substances in all vertebrates, and that of the cod appears to be identical with that of mammals. The question of storage in the invertebrates seems to have been little investigated, but glycogen is common, as it is found in *Pelomyxa* (a rhizopod), the peritoneum of earthworms, the

connective tissue and gonads of molluscs, and the digestive diverticula of crustaceans.

1.5. Vitamins

During the last half-century there has gradually developed the knowledge that the classical constituents of a diet—water, carbohydrates, fats, proteins, and mineral salts—are not by themselves adequate to ensure growth or maintain a healthy life. To the accessory food substances which are required in addition Funk in 1912 gave the name *vitamine*, the terminal 'e' being afterwards dropped when it became certain that the vitamins had no particular connexion with amines. The number of known vitamins increases as research progresses, and some of them are now available in crystalline form and have had probable formulae assigned to them.

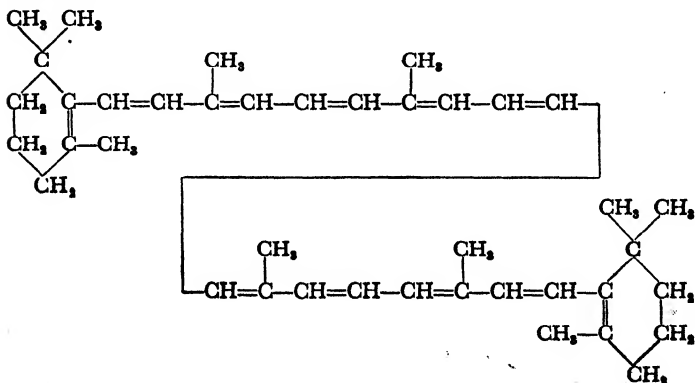
About the method of action of vitamins little is known. There is perhaps no special reason why any physiological generalities should be possible for them, for in their effects they are highly individual. The justification for grouping them together lies merely in the fact that they are not readily identifiable chemical substances, and that their effects are out of all apparent proportion to their quantities. It follows from the latter that they do not exert their effect by any direct contribution to the energy supply, and it is obvious that they have an analogy with catalysts. They differ from the majority of enzymes in that although they are made by plants, animals can make them only in small quantities or, more usually, not at all. Some of them appear to be co-enzymes in oxidation systems. Often their most striking effects are the deficiency diseases caused by their absence, of which some have been shown to be extreme cases of a more fundamental upset in the functioning of the body. A diet poor, but not completely lacking, in a particular vitamin, may cause general ill

development without the presence of any recognizable disease. Adding milk, which is rich in many vitamins, to an institutional diet previously regarded as adequate, caused a gain in growth-rate of 3 pounds in weight and nearly 1 inch in height per boy per year. There is no doubt that a large proportion of the population may get an adequate, but certainly does not get an optimal, supply of vitamins.

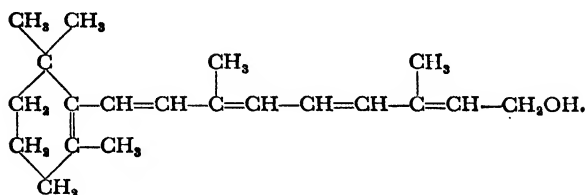
The vitamins are mostly known by the letters of the alphabet, but the few of which the chemistry is known are generally called by definite names. The classification into water-soluble and fat-soluble is probably not important, and so for convenience the list which follows is arranged in alphabetical order.

1.51. Vitamin A, the Antixerotic Vitamin

Vitamin A is fat-soluble, and is present in the waxy part of the fat of both mammalian and fish liver, and to a lesser extent in milk fat and eggs. It is not destroyed by ordinary cooking and keeps well. Since animals can make it from carotin, any food which contains this will serve instead of a supply of the actual vitamin itself. The change, which is probably carried out in the liver, is a simple one; β -carotin, which is



is hydrolysed to two molecules of vitamin A,

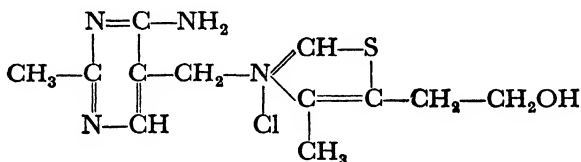


The most striking effects of an inadequate supply of vitamin A are certain defects of the eyes—in children xerophthalmia, an inflammation of the cornea and conjunctiva, and in adults night blindness, an inability to see in twilight. With these are associated other symptoms, particularly in children an increased susceptibility to the common skin infections like rashes and boils. The feature common to all these is an increased keratinization of epithelia, which leads to the disease either directly or indirectly by making it easier for Bacteria to invade the affected part. With such weakened resistance Bacteria not normally pathogenic may become so. A deficiency of vitamin A has other effects, mostly connected with degeneration of cells, including those of nervous tissue. In view of the great effect of nerve-cells on the rest of the body it is possible that this is the fundamental effect, the others, including the keratinization of membranes, being secondary. Vitamin A is chemically closely related to the visual purple of the retina, and night blindness is presumably caused by non-formation of this pigment. It has been claimed that vitamin A has a general anti-infective action, but experimental work points to the conclusion that its protective value applies only to epithelia. As, however, this type of tissue is widespread, and as many of the parasites which infect man must pass through epithelia by their own efforts in order to do so,

the importance of an adequate supply of the vitamin is obvious.

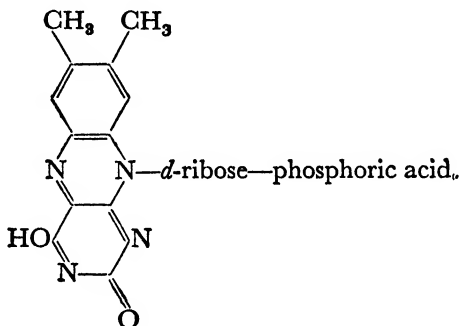
1.52. The Vitamin B Complex

Vitamin B₁, the anti-beri-beri vitamin, or vitamin F or aneurin or thiamin, is water-soluble, and although no foods contain it in large quantities it is widely spread, as it occurs in whole meal, peas, beans, yeast, milk, and eggs. It is not appreciably destroyed by three hours' heating at 100° C., so that dried eggs and wholemeal bread and biscuit are satisfactory sources. At 120° C. it is rapidly destroyed, so that it is absent from canned food. Its formula is

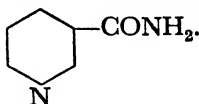


This is the transport form; the active substance, which is the pyrophosphate, is the coenzyme in the oxidation of pyruvic acid. The fact that in experimental B₁ deficiency pyruvic acid accumulates especially in the brain, suggests that this particular type of respiration is of greatest importance in the nervous system, and agrees with the idea that minor nervous disorders are often associated with shortage of this vitamin. The upset of respiration is here the fundamental thing, as it is also in the more obvious clinical deficiency diseases. The chief of these is beri-beri, in which there is muscular wasting, anaesthesia of the skin, and finally paralysis of the muscles. Beri-beri is associated with a diet of polished rice, that is rice with the embryo and pericarp removed, these being the parts which contain the vitamin. Experimentally its deficiency causes similar diseases, particularly polyneuritis in birds.

The original vitamin B₂, or vitamin G, similar in general properties to B₁ but more heat-resistant, has been split into two main factors. The first, lactoflavine or riboflavin, is identical with the non-protein (prosthetic) part of the molecule of the yellow enzyme, flavo-protein, which takes part in oxidation in the cell (p. 85). Its structure is



The other, the anti-dermatitis or pellegra-preventive vitamin or P.P. factor, is nicotinic amide,



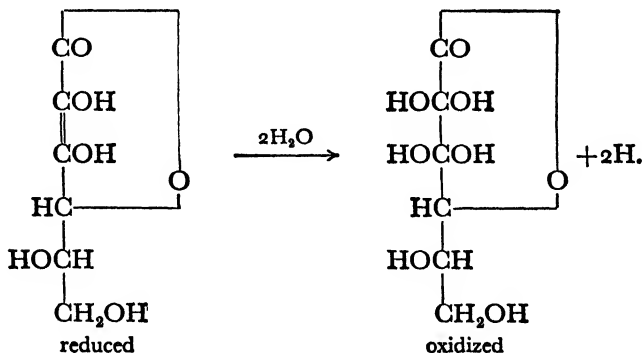
Its absence from the diet causes pellagra, a disease which includes dermatitis of the face, hands, and feet, an inflamed gut, and in its final stages mental disorders caused by changes in the central nervous system. It is almost entirely a maize-eaters' disease, and is very common in the southern states of the United States of America, and followed the introduction of maize into Europe and Africa. Nicotinic amide is important in respiration.

Vitamins B₃, B₄, B₅, B₆, B₁₂, and B_x, occur in association with B₁ and B₂, and are claimed to be necessary for a healthy life in rats or pigeons. Little is known about them.

1.53. Vitamin C, the Antiscorbutic Vitamin, Hexuronic Acid, or Ascorbic Acid

Vitamin C is water-soluble and is found chiefly in fresh fruits and vegetables, but its distribution is not very uniform. The Mediterranean lemon (*Citrus medica* var. *limonum*) is a good source, but the West Indian lime (*C. medica* var. *acida*) is a very bad one. It is very easily oxidized, particularly in alkaline solution; lemon-juice brought to a pH of 12.5 and left exposed to the air loses all its vitamin C in three hours, but at pH 7.0 it is hardly affected by a week's exposure to the atmosphere. Vegetables and potatoes cooked in the ordinary way lose less than half their ascorbic acid, and it is sometimes present in canned or dried foods, if these are acid and have been preserved in absence of air.

It has been synthesized from *d*-galactose, and exists in an oxidized and a reduced form, the formulae of which are



Most animals can manufacture it for themselves, the raw material in the case of rats being probably mannose, but they cannot make it in sufficient quantities and still need an outside supply for a healthy life.

The ease with which it is oxidized suggests that it acts at some point in tissue respiration, and that its absence

leads to a break-down of protoplasmic structure. The chief deficiency disease associated with it is scurvy, which is characterized by haemorrhage of the limbs and jaws. This is presumably caused by an increased permeability of the walls of the blood-vessels. The suggested role of ascorbic acid in this agrees with the general observation that the properties of living membranes are dependent on their respiration.

Ascorbic acid is normally excreted in the urine, but in certain infectious diseases it is found there in smaller quantities than normal, which suggests that it is being used up in the body. It has recently been shown that it inactivates diphtheria and vaccinia virus injected into rabbits. These facts agree with the observation that its absence leads to a reduced resistance to infections. It is possible that it is used in the formation of antibodies.

1.54. Vitamin D, the Antirachitic Vitamin, Calciferol

Vitamin D is fat-soluble, but it is not found in high concentration in any common foods. The best source is fish-liver oil, particularly from the cod, halibut, and tunny. Some is present in egg-yolk, oysters, and mushrooms. Although all these are unusual or expensive foods a deficiency of D is not common except in northern countries, because it is readily formed by ultra-violet irradiation of ergosterol, which is widely distributed. Sunlight is an adequate source of the radiation, and the reaction can take place in the skin of animals, including man. The formulae of vitamin D and ergosterol are uncertain, but they contain only carbon, hydrogen, and oxygen, and contain both benzene rings and aliphatic chains. Synthetic vitamin D prepared in this way is called calciferol.

Deficiency of vitamin D causes true rickets in children of from nine months to two years, adolescent rickets in older children, and osteomalacia in adults. In all of these

there is malformation of the bones, and with this are often associated malformed dentine and tetanic spasms. Rickets can be produced experimentally not only by restriction of vitamin D, but also by a deficiency of calcium or phosphorus in the food, and by an unusual calcium/phosphorus ratio. Rickets is associated with a deficiency of phosphorus in the blood, and the associated tetany with a similar deficiency of calcium, so that it is unlikely that vitamin D acts by increasing the rate of deposition of these in the bone. More probably it increases the net absorption of them from the gut. In rickets nearly all the calcium taken in the food is passed out with the faeces, and so is two-thirds of the phosphorus. In normal animals much smaller quantities are lost. Excess of vitamin D given to dogs reduces still further the amount of these two elements in the faeces, increases the amount in the blood, and leads to increased calcification, and calcification in improper places such as the arteries and kidneys.

The method by which vitamin D increases absorption is unknown. It has no connexion with the secretion of the parathyroid (p. 178) which raises calcium and phosphorus in the blood by abstracting them from bone.

1.55. Vitamin E or X, α -tocopherol

Vitamin E is fat-soluble, but, like A, is present in the waxy, not the fatty, parts of such fats as those of the embryos of seeds, green leaves, and to a lesser extent milk, flesh, and egg-yolk. It is quite stable, but is destroyed in rancid fats. It is an alcohol of the probable formula $C_{29}H_{50}O_2$.

Its absence causes sterility in rats in both male and female. In the former the seminiferous tubules degenerate, the sperms lose their motility, and the animals lose their normal interest in the opposite sex. When all the tubules have degenerated the effect is irreversible. In the female

a lack of E produces defects of the allantois and yolk sac which lead to asphyxia and starvation of the foetus, and its resorption in a late stage of pregnancy. This is a temporary effect, and if E is administered in time the next pregnancy is normal.

Lack of vitamin E in males causes also some of the appearances of castration, and these can be removed by administration of extract of the anterior lobe of the pituitary (p. 179). When E is injected into young females their genital regions hypertrophy in much the same way as when anterior-lobe extract is injected. It is therefore possible that E acts by stimulating the secretion of prolactin (p. 266).

All the detailed work on vitamin E has been done on rats, but there is some evidence of a general kind that it is also necessary in cows, hens, and women. It is unlikely that there is normally a deficiency of it, nor is it probable that an excess of it leads to an increased reproduction rate.

1.56. Other Vitamins

Vitamins H, K, P, R, and S are necessary for a healthy life in chicks, M in monkeys, and L and W in rats. Little is known about them, but K is necessary for correct clotting of blood in man. It is seldom likely to be deficient.

1.57. Vitamins in Invertebrates

There is a good deal of scattered evidence that many invertebrates need accessory food substances in addition to the ordinary constituents of a diet, but not enough is known for it to be possible to generalize. Each of the three common constituents of the B complex has been shown to be necessary for one or more species of insect, but otherwise the relation of the invertebrate accessory factors to the vertebrate vitamins is doubtful.

II

EXCRETION

IN many of the chemical reactions which go on in the animal body, whether their object is to provide energy or to make some definite substance which the animal needs, by-products are formed for which there is no immediate use. Any process by which these by-products are so treated that they take no further part in metabolism is called excretion. The term is not generally applied to the voiding of material which enters the body and passes out unchanged: thus the nitrogen which leaves the lungs of tetrapods, and the undigested cellulose in the faeces of herbivorous animals, are not regarded as excretory products. It is, however, difficult to delimit the latter exactly, and it is obviously impossible in the ordinary way to distinguish between those molecules of a substance such as water which were formed by chemical action in the body, and those which were merely taken in with the food. The analogy with the waste products of a chemical factory is a fairly close one: the method of dealing with the unwanted material depends on its quantity and nature, and the harm which it would do in its place of origin.

2.1. Substances Excreted

For convenience the materials which are excreted may be put into four groups:

2.11. Water

Most animals, whether they live on land or in ponds or in the sea, take in large quantities of water with their food, and mammals and birds drink it as well. Expulsion of this water is not strictly excretion, but some is also formed in the complete oxidation of fats and carbohydrates, and in all the class of reactions called condensations. Further,

the surface of the animal cell is normally a semipermeable membrane and the osmotic pressure of the protoplasm greater than that of fresh water; this means that fresh-water animals will take up water osmotically. Unlike plants, animals seldom have rigid cell walls, and so this last process would, in the absence of special arrangements, go on indefinitely. In such animals the regulation of this osmotic water is more important than the excretion of that from the first two sources; it is considered in section 8.3. Feeding animals with deuterium oxide (heavy water) has shown that there is rapid interchange of water between the gut and the cells. It is, therefore, impossible to distinguish between molecules of water from the three sources.

2.12. Carbon Dioxide

Carbon dioxide is the normal end-product of the carbon of any material which is oxidized to give energy. The organ systems which get rid of it are generally those which bring oxygen into the animal, and so its excretion is considered under the heading of respiration; an account of the chief process in mammals is given in section 3.3. It need only be said here that small quantities are dealt with in other ways, for example, by being converted into urea (p. 38) or calcium carbonate.

2.13. Nitrogen Compounds

Nitrogen compounds are so much more important than the other groups that excretion in many cases means in effect nitrogenous excretion. The metabolism of nitrogen in vertebrates is fairly well known, and although much less is known of other phyla it has been shown that in Annelida, Mollusca, and decapod Crustacea the general type of process is very similar. As has been said on p. 37, excretory nitrogen has two origins: it may be endogenous, that is formed from the break-down of living tissue, or exogenous, derived from proteins which have never actually

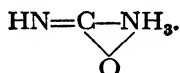
been incorporated in the body. The first type represents waste of the fundamental chemistry of life, the second is merely an unwanted part of the protein molecule. The remaining part is built up to carbohydrate or possibly fat (see p. 38). The first step in exogenous nitrogen metabolism is the separation of the nitrogenous part of the aminoacid molecule as ammonia, a process which is called deamination, and which in vertebrates takes place chiefly in the liver. The ammonia is usually treated in some way before elimination. A list of the chief forms of excretory nitrogen follows; the methods of formation of some of these are discussed on pp. 38-42.

Ammonium may be eliminated in combination with other radicals.

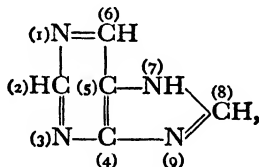
Trimethylamine oxide, $(\text{CH}_3)_3\text{N}:\text{O}$.

Amino compounds, chiefly acids, such as hippuric acid or benzoyl glycine, $\text{C}_6\text{H}_5\text{CO}\cdot\text{NH}\cdot\text{CH}_2\text{COOH}$.

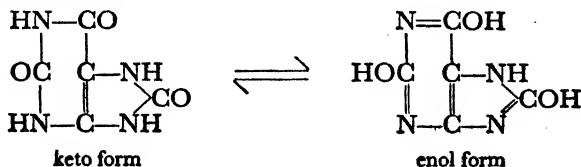
Urea; the usual formula now given to this is that of Werner,



Purine,



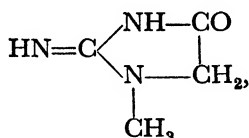
does not occur free in Nature, but its derivatives are common, for example uric acid, a 2-6-8-trihydroxypurine which exists in two forms.



It is not a true acid, but in its enol form it dissolves in alkalis giving monobasic acid urates of the type RHU , dibasic neutral urates, R_2U , and quadriurates, $\text{RHU.H}_2\text{U}$. When it is in solution in animals it is usually in the form of acid or quadriurates, in mammals generally the latter. Purines are largely break-down products of nucleoproteins, but they can also be formed in other ways. Reasons for the conversion of urea to uric acid, the least-soluble form of excretory nitrogen, are discussed on pp. 282-3.

Insoluble protein.

Creatinine,



is the normal form in which endogenous nitrogen is lost in mammals.

It will be noticed in the accounts of excretion in the different phyla (pp. 61-79) that ammonia and amino-acids tend to be eliminated in the greatest concentration in aquatic forms, and urea or purines in terrestrial forms.

2.14. Other Substances

There is scarcely an element which has not at some time been found amongst the excretory products of animals. The inclusion of all substances other than water, carbon dioxide, and nitrogen in one group has no justification except that the remaining substances are quantitatively much less important. Qualitatively they may be just as important to the animal as nitrogen. The chief are phosphorus, usually as phosphate, sulphur as sulphate, and calcium. They are generally eliminated by the mechanism which deals with nitrogen.

2.2. Methods of Excretion

The object of excretion is to remove from the sphere of chemical action of the body end-products which may be harmful, and which in any case will, if they are allowed to accumulate, upset equilibrium by their mass-action effect. The simplest way to do this is by a method sometimes used in the treatment of poisoning, that is by converting the obnoxious substance into some insoluble derivative. In this state it can do no harm. Any part of the body which seems to be specially used for storing such materials is sometimes called a 'kidney of accumulation', though there is no suggestion that there is any similarity to the mammalian kidney other than very generally in function.

It is possible that in some cases such insoluble waste products, originally quite useless, have become of some benefit to their possessors. It is noteworthy that many skeletal materials contain elements which are often excreted. Chitin contains 4 per cent. of nitrogen, calcium carbonate is a form of carbon dioxide, and bone is largely made of calcium phosphate, itself a common excretory product. It is impossible to be dogmatic as to whether a particular substance is primarily excretory or useful, but in some cases the probability is great on one side or the other. For example, it may safely be said that the uric acid which forms the chief pigment of butterflies of the family Pieridae (the Whites) was primarily excretory in origin, and that it is a peculiarity of the group to have found a use for so normal a waste substance.

Even where excretory products are made insoluble and stored they usually sooner or later escape to the exterior and are lost. Exoskeletons are shed, and insoluble material in the coelom goes out by pores. But more often there is some definite mechanism by which the unwanted material is voided. The word 'kidney' has often been applied to any organ which appears to be concerned in this, but it seems

better to restrict the word to the particular type of organ which carries out nitrogenous excretion in the vertebrates. Alternative names are available in all groups, and 'excretory organ' is good enough for general purposes.

The morphological nature of the excretory organ varies from group to group. Details of structure may be found in the ordinary text-books of zoology, but some general classification is necessary to render intelligible what follows.

First, the surface of the body may be used, either, as in Protozoa and coelenterates, the unspecialized cell surface, or, as in the skin of man, an epithelium specially developed into such glands as the sweat glands.

In many invertebrates the nephridium is important. This is an ectodermal derivative, centripetal in growth, with an intracellular lumen, and primarily ending in a flame cell (solenocyte). It is found in Platyhelminthes, Rotifera, Annelida, Mollusca, and *Branchiostoma*, and it is customary to consider it homologous in all these. The classification of nephridia is not a matter for a book on physiology, but it may be said that they are called proto-nephridia if they do not open into the coelom, and meta-nephridia if they do. The external opening of a nephridium is a nephridiopore, and the internal opening of a meta-nephridium a nephridiostome.

Some authors consider that the original function of the coelom was to store excretory matter. However that may be, excretion is often carried out by coelomoducts, which are paired structures almost exactly opposite to nephridia in their properties. They are mesodermal, centrifugal in growth, have an intercellular lumen, and do not have flame cells at their ends. They are found in Annelida, Mollusca, Arthropoda, Echinodermata, and Chordata, and are considered homologous in all these groups. Although they were probably evolved as genital ducts, in all these phyla they also assist in excretion.

In some cases, particularly the polychaetes, nephridium and coelomoduct are closely associated to form a compound organ, the nephromixium. This may retain both genital and excretory functions, or may be excretory only.

In many animals the gut is excretory, and in a few cases (Crustacea, insects, spiders) a diverticulum of it is the chief organ. It is doubtful whether the specialized structures in the different groups can be regarded as homologous.

There remain a few special types which can be put in none of the above groups. They are mainly small organs in which waste products accumulate. The fat body of insects is an example.

2.3. The Vertebrate Kidney

By far the best known of all excretory mechanisms is the vertebrate kidney. It eliminates water, nitrogen, and many other substances, and has shown itself capable of adaptation to very varied circumstances. In addition to dealing with waste matter it is also an important osmotic regulator; this aspect of its function is dealt with in section 8.3. Although its structure varies to some extent with the evolutionary level of its possessor (it is a mesonephros in fishes and Amphibia, and a metanephros of somewhat different origin in the amniotes) and also with the environment, it is always built on the same general plan. It consists of a mass of coelomoducts opening into a single longitudinal collecting duct. The detailed arrangement in the mammals is as follows (Fig. 9). The coelomoducts have lost their original openings to the general coelom, and each starts as a blind Bowman's capsule. In the cavity of this is a bundle of blood capillaries, known as the glomerulus, derived from the renal artery. Bowman's capsule and the glomerulus are together known as the Malpighian body. From Bowman's capsule the coelomoduct continues

as a coiled proximal convoluted tubule, then as the loop of Henlé, and finally as the distal convoluted tubule. Several of the latter open into one collecting tubule, and this joins with others to form large ducts which finally open into the ureter. The whole part distal to Bowman's capsule is spoken of collectively as the tubule. Blood is brought

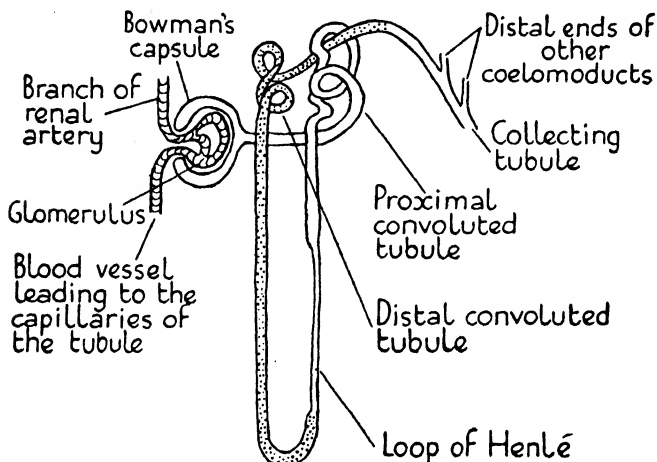


FIG. 9. Diagram of a single coelomoduct of a mammalian kidney.

away from the glomerulus by a single vessel which breaks up into another set of capillaries surrounding the tubule. From them blood goes into the renal vein. There are some differences from this structure in other classes of vertebrates; the marine teleosts either have a much reduced glomerulus or are without it altogether, and in those animals which have a renal portal system the tubules (but not the capsules) are supplied with a second system of capillaries containing venous blood.

The difference in histological structure between the capsule and the tubule, and the absence of the glomerulus in some groups, suggest that these two parts of the kidney

have different functions; there is now no doubt that this is the case.

In the Amphibia and Reptilia it has been possible by means of a micromanipulator to withdraw small samples of the fluid from a capsule for analysis. This 'glomerular transudate' (the reason for the name will appear shortly) has been found to resemble a fluid obtained from the blood by dialysis; with respect to every constituent for which the former can be analysed they are identical, and their electrical conductivities are the same. There is thus little doubt that the fluid in the capsule is blood plasma without its colloids. The only assumption that need be made to explain how this comes about is that the wall of the glomerulus together with that of the capsule acts as a membrane which is impermeable to colloids but permeable to water and crystalloids; that is, as a dialyser. If this is the case the conditions in the Malpighian body are that a membrane impermeable to colloids has water, crystalloids, and colloids on its one side, and water and crystalloids on the other. The ordinary laws of osmosis apply, and in the absence of any outside forces, water and crystalloids would pass through the membrane into the blood under the influence of the osmotic pressure of the colloids. But in fact they travel in the other direction, and this can only happen if there is a hydrostatic pressure acting in the opposite direction to the osmotic pressure. This is normally always present, since the blood is maintained above atmospheric pressure by the pumping action of the heart. Filtration should stop when the hydrostatic pressure in the glomerulus falls below the osmotic pressure of the colloids. This is the case; in mammals the colloids have an osmotic pressure of about 30 mm. of mercury, and secretion of urine ceases when the arterial pressure falls below about 40 mm. (It is to be expected that the pressure in the capillaries will be somewhat less than that in a large

artery such as the brachial where blood-pressure is usually measured.) Secretion may be stopped experimentally by ligaturing the ureter; in one experiment it ceased when the pressure in the ureter was 92 mm. of mercury and that in the arteries was 133 mm. The difference, 41 mm., is obviously the maximum pressure available for forcing water and crystalloids out of the blood under these conditions, and it was just not enough to do so. The converse experiment, to increase the effective filtration pressure, has also been carried out; a certain volume of blood is removed, and replaced by Ringer-Locke fluid, which is isotonic with the blood but which contains no colloids. Under these circumstances, although the blood-pressure actually falls owing to the shock, the rate of excretion greatly increases.

Since the energy for the filtration comes from the heart, one would not expect an alteration in excretory rate to affect the oxygen consumption of the kidney. This is found to be the case. Furthermore, it would be expected that low temperature or respiratory poisons, while reducing those activities of the kidney which alter the composition of the glomerular transudate, would not greatly affect the glomerulus. The urine would therefore have a much closer resemblance to the original glomerular transudate than it normally does. This also has been experimentally confirmed, and at 25° C. or when cyanides are added to the blood the urine (in excised and perfused dogs' kidneys) is very similar to the dialysate from plasma.

In the Amphibia there is thus direct evidence, and in the mammals good circumstantial evidence, that the Malpighian bodies act merely as ultrafilters which separate water and crystalloids from the plasma. By adding various proteins to the blood and observing if they appear in the urine, it has been found that the distinction is not strictly between crystalloids and colloids, but that the membrane

is permeable to molecules of smaller molecular weight than about 70,000. Gelatin, of molecular weight 35,000, and haemoglobin, of molecular weight 67,000, are passed out, while the normal serum proteins of molecular weight of not less than 72,000 are retained. There is evidence that in dogs about 20 per cent. of the total plasma flowing through the kidney is filtered. This would correspond to something over 100 ml. per minute in man.

There remains the question of the part which the tubules play in excretion, and here the story is not so simple. Not only is the urine more concentrated than the glomerular transudate, but its composition is different. In the Amphibia, where the two can be directly compared, the urine is poorer in chloride, sodium, and potassium, contains no glucose, and is richer in urea and other waste products. If we assume that the glomerular transudate has the same crystalloid composition as the plasma, the same holds for mammals. The alteration could be brought about by absorption of water and differential absorption of the solutes, or it could be achieved at least in part by specific excretion of the different substances. In either case the urine would be concentrated and work would be done on it, so that oxygen would be needed. There is evidence showing that both processes go on. It is possible to collect and measure the fluid from a single Bowman's capsule in the frog, and since the total number of capsules is approximately known the rate of filtration per kidney can be calculated. It is found to be at least ten times the rate of urine formation, so that 90 per cent. of the filtered water must be absorbed. In man the rate of filtration calculated on the assumption that each glomerulus has the same capacity as in the frog is at least a hundred times the rate of excretion of urine, but this is probably largely because not all the glomeruli are normally working at one time. Since glucose, chloride, and some others are decreased in

concentration at the same time, it is obvious that they must be absorbed too. According to the older view the substances in the transudate can be divided into two classes. 'Threshold substances' are normally all absorbed, but if their concentration in the blood (and so in the capsular fluid) rises to a certain threshold value the tubule is incapable of absorbing them fast enough, so that some appears in the urine. To this class belong glucose, and also sodium chloride, although a little of this is normally present in the urine of mammals. The 'no-threshold substances' are not absorbed and so are excreted whatever their concentration in the blood; the sole effect which the tubules have on them is to concentrate them by absorbing water. Urea, other nitrogen compounds, and sulphate are examples. It is now considered probable that there are no true no-threshold substances, but that all are absorbed to some extent. The distinction between high-threshold and low-threshold substances is, however, a real one, and it is perhaps helpful to regard the tubules as absorbing a sort of ideal plasma, rich in the important substances such as glucose, chloride, and phosphate, and poor in waste products. The extent of the absorption is limited by the force which the cells can exert, and it has been found that the limiting osmotic pressure against which the human kidney can absorb is about 25 atmospheres. Any substance, such as urea, which is itself only absorbed to a small extent, must raise the osmotic pressure of the filtrate and so act as a diuretic; that is, it increases the volume of urine formed. By analysis of fluid drawn from different parts of the frog's kidney it has been shown that absorption goes on in both convoluted tubules, but that most of the glucose is absorbed in the proximal tubule and most of the chloride and water in the distal tubule.

Finally, it must be asked whether or not the tubules add anything to the urine as it passes through them. There is

plenty of evidence that they do. The cells lining the tubule are of several different kinds, and this suggests different functions, one of which might well be excretion. In marine teleosts there is no glomerulus, yet the urine contains waste products which can only have come from the blood through the tubules. There seems now to be little doubt that the renal portal vein of the frog goes only to the tubules. If the renal artery is ligatured, and the animal kept in oxygen to raise the oxyhaemoglobin content of the venous blood, excretion stops. If, however, urea be injected into the blood, it is excreted, together with some water. Further evidence comes from the argument that if the filtration be increased by any means, there should, if the tubules do nothing but absorb, be an equal effect on the amount of all the excretory products. But this is not the case. For example, owing to alterations in the pressure in the kidney there is increased filtration, with consequent diuresis, in the recumbent position in man. The output of water in one experiment went up 237 per cent., that of chloride 123 per cent., of phosphate 50 per cent., of sulphate 41 per cent., of urea 64 per cent., and that of ammonia not at all. It follows that the solids must be in part excreted by the tubules, and that they are the sole source of the ammonia, although some workers disagree.

The action of the tubules in adding excretory substances to the blood is often called secretion, but the word is best used only in connexion with an organ which actually prepares a definite chemical substance which is used by the body.

The tubules are continually doing work, and so require oxygen. The glomerulus also requires oxygen to maintain the dialysing properties of the membrane. The respiratory quotient (see p. 81) of the kidney is between 0.8 and 0.9, and it can oxidize carbohydrate, protein, and fatty derivatives; which of these it normally uses is unknown.

The kidney is obviously greatly dependent on vasomotor stimuli, since these affect the blood-pressure, but beyond this its control is complicated. Dilution of the blood after drinking much water would necessarily cause diuresis by lowering the osmotic pressure of the colloids and so increasing the effective filtration pressure, but diuresis occurs without any measurable dilution of the blood, and where dilution and diuresis can be demonstrated together the two do not run parallel with one another. Whatever the exact mechanism of the control may be, the posterior lobe of the pituitary is possibly important, as pituitrin increases absorption of water by the tubules. There is also some correlation with other forms of water loss; in the tropics, where white men presumably sweat more than in their native land, their urine production is only 50 per cent. of the normal.

The urine passes to the bladder through the ureters, which have walls containing plain muscle, and which in man have about three waves of contraction passing down them per minute. The bladder can hold a gradually increasing volume of urine without showing any increase of pressure or of muscle tone. The act of micturition, voluntary in origin unless the bladder is over-full, is assisted by several involuntary muscles, and results in the complete emptying of the bladder.

The urine is the chief channel by which nitrogen escapes from the body, in whatever chemical form the metabolism of the animal may leave it (see section 1.41). In man, of the 60 gm. of solid passed in the urine in the 24 hours, about 35 gm. are made up of organic nitrogen in various forms. The sulphur obtained from the cysteine part of the protein molecule appears as sulphate to the extent of about 2.5 gm., and there are about 3 gm. of phosphate measured as phosphorus pentoxide. About 8 gm. of chloride are present, though as this is obtained unchanged

from the food it is not strictly an excretion. The chief bases present are potassium and sodium, of which there are about 3 and 5 gm. respectively. All these values vary widely with the food. Other metals, notably calcium, magnesium, and iron, are present, but only in small quantities.

2.4. Other Vertebrate Excretory Organs

Waste products may pass to the exterior through other channels than the kidneys. Water leaves by the skin, from the lungs, and to a small extent in the faeces. Carbon dioxide, mainly lost from the lungs, is dealt with in section 3.3. About half the magnesium and calcium and most of the iron leave through the intestine, the two former being mainly in the form of insoluble phosphate and the last chiefly sulphide. A small amount of nitrogen, about 1 gm. per day in man, also goes out in this way. It is largely in the form of bile, which contains break-down products of haemoglobin. The sweat contains most of the common excretory substances, but in negligible quantities. There seems to be no excretion by storage in the vertebrate, but the calcium phosphate of bone and the keratin of hair and scales may perhaps be regarded as waste products which have been put to some use. This is certainly the case with the urea in the blood of elasmobranchs, which, as shown in section 8.3, serves to maintain the plasma isotonic with sea-water.

In the embryos of the amniotes the allantois is used as a deposit for renal waste which has been eliminated by the mesonephros. In those mammals where the placenta is highly permeable (e.g. rodents and man) the excretory products are apparently simply taken away by the maternal blood; the mesonephros has only a very short existence, and the allantois is a functionless stalk or (as in the mouse and rat) never develops at all.

In the teleosts most of the ammonia and urea which are formed are lost through the gills, the chief forms of nitrogen in the urine being creatine, creatinine, and trimethylamine oxide. This is connected with the marine habitat (see section 8). The elasmobranchs are somewhat similar, but the gills are much less permeable to urea, which is largely retained in the blood.

2.5. Excretion in Invertebrates

2.51. Excretion in Protozoa

There is no uniformity in the nitrogenous waste products formed; *Amoeba* forms uric acid, *Paramecium* and *Spirostomum* urea, and *Glaucoma* and *Didinium* ammonia. These products have been shown to accumulate in cultures of the animals named, but there is no evidence to show how they came to be outside the animal. The old story that the contractile vacuole is a specific excretory organ rests on a very insecure foundation, since attempts to show the presence in it of nitrogenous waste have failed. One author, for example, knowing the rate at which urea accumulated in a culture of *Paramecium caudatum*, and the rate of elimination of water by the vacuoles, was able to calculate that if all the urea excreted came from the vacuoles its concentration in them should be one part in from 2,000 to 3,000. He injected into the vacuoles Nessler's solution and other reagents sensitive to one part in 12,000, but his results were negative. It is therefore probably sufficient to assume that soluble waste products diffuse out through the whole cell wall, just as it is assumed that carbon dioxide can diffuse out and oxygen can diffuse in. The contractile vacuole undoubtedly eliminates water, which probably contains waste products in solution, so that to a certain extent it assists in excretion, but it cannot be responsible for the whole or even a major part of it. Analysis of the fluid removed from the contractile vacuole

of *Spirostomum* shows that it only eliminates 1 per cent. of the total urea produced.

It is probable that some of the crystals found in many genera are waste products stored in an insoluble form; in *Paramecium caudatum*, for example, granules of acid calcium phosphate have been demonstrated. The shells of Protozoa, which may be of calcium carbonate, strontium sulphate, silica, or a nitrogenous material, may be regarded as excretory; this view seems particularly likely to be correct where, as in *Polystomella*, most of the protoplasm is outside the shell, which can therefore hardly be protective.

2.52. Excretion in Coelenterata

Most chemical investigations have been negative, but uric acid has been found in *Anemonia sulcata*, and urea in other sea-anemones. There are no specialized excretory organs, and it must be assumed that waste products escape as they do in the Protozoa. In actinians it has been shown that injected substances, such as carmine, accumulate in certain regions, and this may mean that these places are specially active in excretion. Skeletons are common, both of calcium carbonate, as in the corals, and of nitrogenous organic material, as in the perisarc of Hydrozoa and in the gorgonians (Actinozoa). One function of the symbiotic green Algae in corals seems to be to remove end-products, such as carbon dioxide.

2.53. Excretion in Platyhelminthes

The flame-cell system, termed a protonephridium, and regarded as the forerunner of the nephridium of annelids, is usually regarded as the excretory system. It certainly expels a fluid, but the chemical investigations of this are few and unsatisfactory. There is some evidence that the nephridia are also osmotic regulators (e.g. their absence

from the Turbellaria Acoela, which are all marine; variation in the rate of pulsation of the terminal vesicle in Cercariae with the external osmotic pressure; see section 8.3). It has, however, been recently shown that this is not the case in *Gunda ulvae*.

2.54. Excretion in Annelida

Ammonia is the chief form of nitrogenous excretory product in the polychaete *Aphrodite* and in the medicinal leech, but in the earthworm *Lumbricus agricola* this makes up only 20 per cent. of the total, 40 per cent. being urea and the rest aminoacids, purines, and unidentified compounds. The nephridium was probably from its inception excretory in function, but it has in most species come into close relation with a coelomic funnel to form a nephromixium. The nephridium or nephromixium is certainly not the only, and probably not the chief, organ of excretion. The methods of excretion in the lumbricids are as follows:

The cells of the coelomic epithelium covering the gut are modified as chloragogen cells (Fig. 10), containing yellowish granules called chloragosomes, which consist largely of guanine, a purine derivative (formula p. 40). The bases of the cells are always in contact with either the dorsal vessel or a branch of the intestinal plexus, and they probably separate excretory matter from the blood, and perhaps from the coelomic fluid. They fall off into the coelom and act as a kidney of accumulation. The chloragogen cells contain glycogen, but the part which they play in connexion with this is disputed. It is possible that they manufacture it from fatty acids, and then hand it on to the coelomic fluid, whence it goes to the tissues.

Other cells of the peritoneum, not near blood-vessels, are known as uric or bacteroidal cells, because they contain rod-shaped bodies, probably of uric acid. They also act as a kidney of accumulation.

Both these types of cell disintegrate, and the insoluble particles which they contain are ingested by amoebocytes of the body cavity. These phagocytes may wander to the

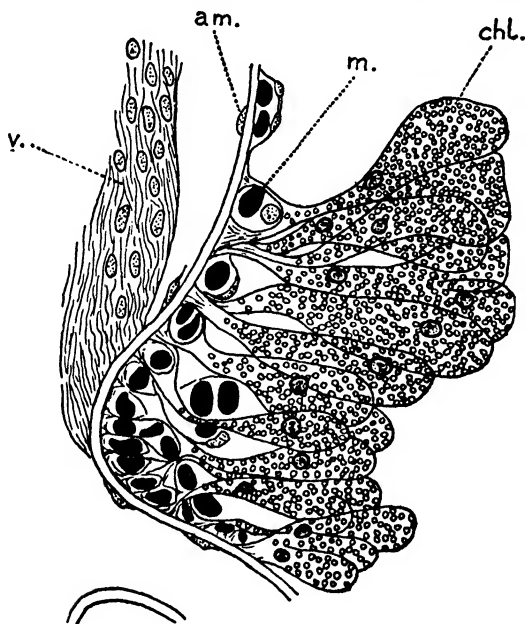


FIG. 10. Horizontal section through wall of dorsal vessel of *Allolobophora transoadiana*; the origin of one of the lateral vessels is seen.

am., amoebocyte of the blood, attached to the inner surface of the 'cuticle' of the wall of the dorsal vessel; *chl.*, chloragogen cells; *m.*, circular muscle-fibre of the dorsal vessel; *v.*, valve, in the lumen of the dorsal vessel. After Rosa.

tissues and deposit their contents as pigment, or they may find their way to the surface and be lost from the body. In some species they collect as masses in the coelom, the 'brown bodies'. These, which may be up to 5 mm. long, are found chiefly in the hinder segments, but they may occur in the genital segments and in the seminal vesicles. In addition to excretory particles they contain cysts of

nematodes and of *Monocystis* and other gregarines, and shed setae. They disappear sooner or later, having probably escaped through the dorsal pores.

Phagocytes in the blood take up excretory matter and carry it to the gut wall, where they stay and become known

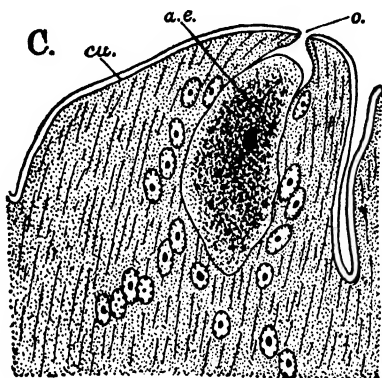


FIG. 11. Section of the oesophageal wall of *All. foetida*, showing a yellow cell or excretory amoebocyte in the act of traversing it.

× 500. *as.*, amoebocyte; *cu.*, cuticle of oesophageal epithelium; *o.*, opening in the oesophageal wall through which the amoebocyte will pass into the lumen of the alimentary canal. From Keilin in the *Quarterly Journal of Microscopical Science*, vol. 65 (1920).

as yellow cells (Fig. 11). They finally fall into the gut lumen and escape with the faeces. (In some books there is confusion between the chloragogen cells and the yellow cells, but the two are quite distinct.)

The nephridium of the earthworm has been shown to be a true nephridium without any mesodermal elements (Fig. 12). Its physiology is unfortunately not so well known, since observers are not in complete agreement, but certain points are fairly clear. In the first place, coelomic fluid and the finest solid particles which it contains go down the nephridium to the exterior; in lumbricids chloragogen particles are much too large, but this

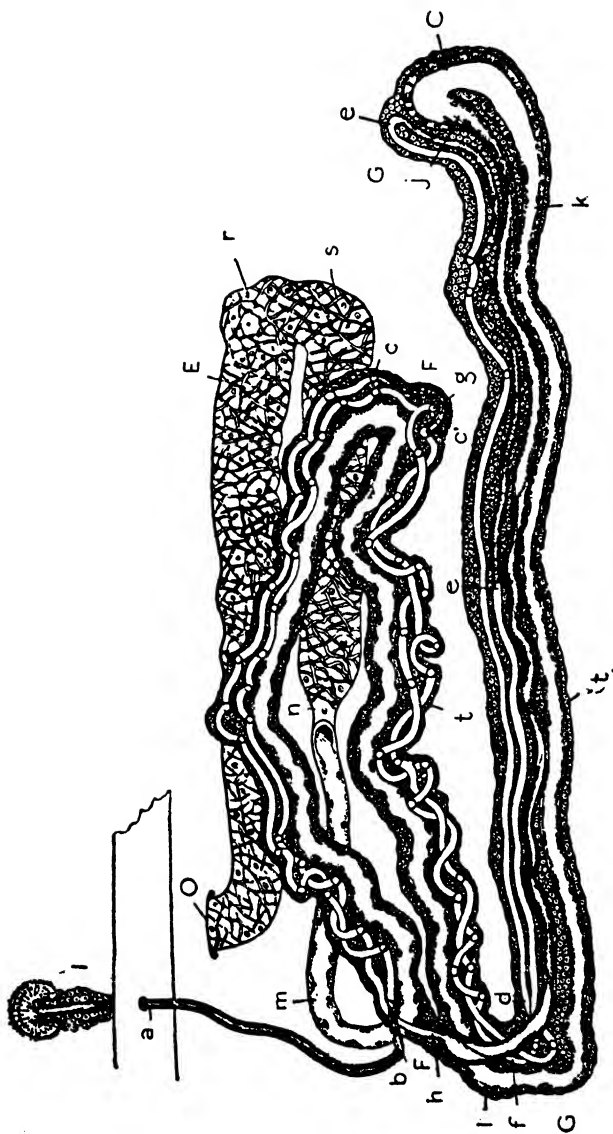


FIG. 12. Nephridium of *Lumbricus*.

a-h, the narrow part of the tube partly ciliated; *h-j*, ciliated wider tube expanding at *C* into ampulla; *k-n*, wide tube; *E*, muscular duct; *I*, funnel; *O*, external orifice; *t*, peritoneal layer; *s*, muscular fibres; *r*, nucleus of cell; *F*, *G*, second and third loops of nephridium. From Benham in the *Quarterly Journal of Microscopical Science*, vol. 32 (1891).

does not apply to the whole phylum. Secondly, cells of the middle tube and the ampulla extract particles of guanine from the coelomic fluid and store them, although they gradually disappear. Experimentally, these cells have been shown to take up particles of Chinese ink and coloured fluids which pass the nephridiostome. One author states that the chloragogen cells transfer waste matter from the coelom to the blood and thence to the nephridia, but most think that the capillaries are solely for supplying oxygen. Thirdly, there is intracellular excretion of granules, through the wall of the terminal reservoir to its cavity. The nephridium empties at intervals of not less than three days.

2.55. Excretion in the Arthropoda

Very little work has been done on the Crustacea except in decapods, where the chief forms of nitrogenous excretory products are ammonia and amino compounds. The antennary gland of Malacostraca and the maxillary gland of Entomostraca, both of which are coelomoducts, are usually described as the excretory organs, but the liquid extracted from the green gland of decapods often contains less non-protein nitrogen than does the blood. It has, therefore, been suggested that in freshwater forms it acts as an osmotic regulator, but since it is also present in the marine species, that cannot be its only function. In *Cancer* the hydrostatic pressure of the body fluid is greater than the colloid osmotic pressure of the blood, and there is filtration of water and crystalloids followed by resorption of some ions and excretion of others, as in the vertebrate kidney. Other forms are probably similar, and the resorption is specially important in the freshwater crayfish and the estuarine shorecrab. The liver was shown long ago to be excretory, for its cells can extract foreign matter from the blood and eliminate it through the gut. In *Cancer* and some other

genera it normally deals with purines in this way, but these could not be found in the crayfish. The exoskeleton, of chitin and calcium carbonate, may be in part excretory, and chromatophores of Eriocheir contain uric acid.

In insects uric acid is the normal nitrogenous excretory product, but ammonia, urea, and amino compounds are found in the clothes-moths, and ammonia is the chief product of dipteran maggots. Guanine is unknown.

The Malpighian tubules, the standard excretory organs of the morphologists, actually are the most important part of the body in disposing of waste matter: they excrete both urates and carbon dioxide, which they receive from the blood in solution. The mechanism bears certain similarities to that in vertebrates, particularly birds; in *Rhodnius prolixus* (Rhynchota), for example, potassium or sodium urate is secreted in the upper part of the tubule, and water and base are resorbed in the lower part, leading to the precipitation of free uric acid as solid spheres. The same water and base are circulated and used repeatedly. This leads to conservation of water, which is very important in insects, where the method of respiration leads to much evaporation. An analogous process leads to the precipitation of calcium carbonate. There is normally no special mechanism for the expulsion of the contents of the tubes, but in Diptera they are muscular and peristalsis takes place.

There are subsidiary organs, of which the chief is the fat body, the parietal layer of which stores uric acid. The fate of this is different in different orders of insects. In the Collembola, which have no Malpighian tubules, it is stored throughout life, and the fat body is therefore the chief excretory organ. It is also stored throughout life in the Orthoptera, where the Malpighian tubules contain little or no uric acid. In the Hymenoptera it is transferred to the hind-gut during early imaginal life, and is voided

when the insect emerges from the cocoon. A similar process occurs in muscid Diptera; here there is a period in metamorphosis when the tubules are completely broken down, and the fat body is therefore very important. Of less importance are the nephrocytes, chains of cells along the heart or oesophagus, which store nitrogenous matter which may later be taken away by phagocytes.

There are in many insects peculiar types of excretion, as, for example, in the celery-fly, *Acidia heraclei* (Diptera), where the calcium carbonate formed in the Malpighian tubules is deposited as large calcosphaerites, is dissolved during metamorphosis, and is laid down on the last larval skin and so eliminated—a process called ecdysial excretion. In some Dipteran larvae calcosphaerites formed in the fat body are eliminated in the same way. As in the Crustacea, chitin may be excretory, and in butterflies of the family Pieridae (the Whites), uric acid formed during larval life is stored in the fat body and shortly before the emergence of the imago it is transferred to the wings and deposited as the familiar white pigment.

In spiders the Malpighian tubules are undoubtedly excretory. They contain uric acid, probably as a sodium salt, and guanine. It is probable that the coxal glands eliminate urates.

2.56. Excretion in Mollusca

In lamellibranchs, ammonia and amino compounds are the chief forms of excretory nitrogen, but urea and purines, including traces of uric acid, have been found. Sixty per cent. of the waste nitrogen of *Anodonta cygnea* is eliminated as ammonia. The concretions in the organ of Bojanus consist mostly of magnesium and phosphate, and uric acid is not present, but there is some nitrogenous material. Keber's organ acts as a kidney of accumulation, but in what form nitrogen is stored is not known. Of the

gastropods, *Helix pomatia* eliminates ammonia, amino compounds, urea, uric acid, and other purines, all in considerable quantity, some at least of them being got rid of by the kidney. In hibernation, uric acid and other purines are stored in the kidney. The slug *Limax agrestis* excretes chiefly urea, and the marine *Aplysia limacina* ammonia, amino compounds, purines, and urea, in that order of quantity. The urine of cephalopods contains much ammonia, trimethylamine oxide, and amino compounds, and smaller quantities of urea and purines. The molluscs illustrate very well the connexion between the habitat and the chief excretory products which was pointed out on p. 58.

Both in lamellibranchs and gastropods the cilia of the kidney withdraw water from the pericardium, but while in the former there are contractions of the organ which expel its contents, in the pulmonates general contractions of the body are required for its discharge. In terrestrial forms these occur every two or three weeks. In *Anodon* and *Limnaea* the urine is hypotonic to the blood and pericardial fluid, but this does not prevent its being excretory (cf. the glomerular transudate of vertebrates, p. 63).

2.57. Excretion in Echinodermata

The fluid of the water-vascular system contains small quantities of ammonia, amino compounds, and urea. Since it is in communication with the surrounding seawater, nitrogen is presumably lost from it.

III

RESPIRATION

IN ordinary usage, and very often as used by physiologists, the word 'respiration' means simply sucking air into the body and blowing it out again: it is in fact synonymous with breathing. It was early recognized that the object of breathing was that the animal might absorb oxygen and give off carbon dioxide, and respiration was extended to cover this gas exchange even where, as in the earthworm, it takes place without any special bodily movement. But further it became obvious that this taking up of oxygen from the atmosphere and giving up of carbon dioxide were simply the beginning and end of a process common to all animals (and indeed to all living matter) by which energy was made available for use. In plants, where there is no breathing, respiration has long meant merely the exothermic chemical changes by which energy is supplied, even when oxygen takes no part in them. It must logically be taken to include comparable processes in animals. Animal respiration, then, is fundamentally an exothermic chemical reaction (or series of reactions) by which energy is supplied for the use of the organism: where oxygen is required for this the whole mechanism whereby the gas is supplied is included in the term, and where carbon dioxide is a by-product of the reaction its removal is included. The word is not used in connexion with the supply of reactants other than oxygen, nor with the removal of products other than carbon dioxide. This limitation may seem arbitrary, but in practice it works well.

At its narrowest, then, respiration means breathing, and at its widest, provision of energy. In most writings on animal physiology it has a meaning between these two in

content, for it generally signifies provision of energy by a reaction involving molecular oxygen; since, as is described below, free oxygen usually only comes into the last of a series of reactions, this limitation is not very helpful. When it is used, the processes described below under the heading of anaerobic respiration are designated by a term which describes their general chemical nature; glycolysis, for instance, is the anaerobic splitting of the hexose molecule. If 'anaerobic respiration' be not used, there seems to be no general term for these processes, unless one uses fermentation, which seems singularly inappropriate for a reaction in which neither carbon dioxide nor ethyl alcohol is produced, zymase is not used, and even sugar may not be. The triple meaning of respiration is unfortunate and at first confusing, but it is usually sufficiently obvious from the context in what sense the word should be taken.

Since an animal is continually doing work in moving itself and other objects, and in secretion, it is obvious that it requires energy. We do not know of any means other than chemical reactions by which this energy can be supplied, so that respiration in the inclusive sense given above is necessary for all animals.

3.1. The Chemistry of Respiration

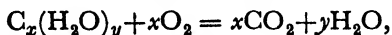
3.11. Aerobic Respiration

Most respiration involves the consumption of oxygen and the production of carbon dioxide, and for a preliminary investigation it is usual to measure the volume changes for these two gases. The experiment is easily carried out with some form of manometer. The ratio

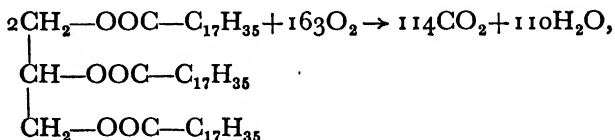
$$\frac{\text{volume of carbon dioxide given out in time } t}{\text{volume of oxygen absorbed in time } t}$$

(both being measured under the same conditions) is known as the Respiratory Quotient, usually abbreviated to R.Q.

Since the volume of a gas, under given conditions of temperature and pressure, is proportional to the number of molecules it contains, it is easy to calculate the theoretical values for the chief classes of foodstuffs, assuming complete oxidation to occur. Thus for all carbohydrates the equation is



and it is obvious that the R.Q. is unity. Tristearin, a common fat, gives



which makes the R.Q. $114/163$, or 0.70 . Other fats give very similar values, and while the figure for protein is more variable, it is always about 0.8 or a little more. The fact that these values are characteristic provides a simple test for the similarity of two processes. For example, the R.Q. of muscle is 1 , that of cilia is 0.8 ; the chemistry of the respiratory processes in the two must therefore be different. It is not possible to argue rigidly from the observed respiratory quotient to the substrate which is being burnt, because a mixture of carbohydrate and fat will obviously give a similar value to protein, and because there is always the possibility of incomplete combustion. The latter is particularly likely where an animal is under peculiar metabolic conditions. In the hibernating dormouse the carbon dioxide production falls to 1 per cent. of the normal, substances like ketones and organic acids are produced instead, and the R.Q. is 0.23 . Other hibernating animals are similar; the R.Q. for the hedgehog is 0.51 . When animals are putting on fat this substance is being formed from carbohydrate, a change which makes internal oxygen available. (This is evident from an ex-

amination of the formulae; in a carbohydrate molecule enough oxygen is present to oxidize all the hydrogen, but in tristearin there is only enough to oxidize about one-sixth of the hydrogen.) Where the food is poor in fat, as in herbivores, this is very noticeable, and in fattening stock the R.Q. is 1.3. The normal R.Q. for man is 0.85, which suggests that carbohydrate is an important source of energy, but that either fat or protein or both are used as well. That the last is the case is shown by the fact that the quotient can be altered within limits by eating any one of the three classes of foodstuff in excess.

If oxygen is taken as the unit the energy available is not greatly different for the three foodstuffs. Thus

1 gm. of oxygen oxidizes carbohydrate to water plus carbon dioxide giving 3.53 Calories,

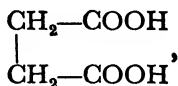
or fat to water plus carbon dioxide giving 3.28 Calories,

or protein to water plus carbon dioxide giving 3.14 Calories.

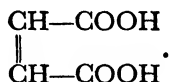
But since 1 gm. of oxygen will oxidize 0.94 gm. of glucose and only 0.17 gm. of tristearin, fat is evidently a much more economical form in which to store energy. A mammal which had its fat replaced by an equivalent amount of glycogen would be very bulky.

The actual process of oxidation, sometimes called cell or tissue respiration, is a chemical reaction involving at least one enzyme and often more than one. In addition a carrier for hydrogen or oxygen is usually required; these carriers are organic catalysts, but they are not generally called enzymes because they are not thermolabile. The best known of them, and the most important, is cytochrome, a substance which consists of the base haem attached to a protein. It can exist in two forms, oxidized and reduced, and the change from one to the other is accompanied by a change in valency of the iron which it contains. It is found in practically all living cells except anaerobic

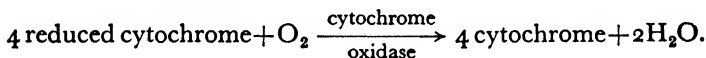
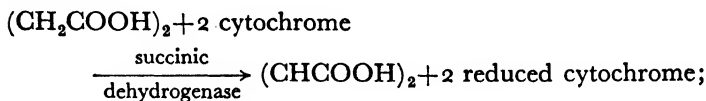
Bacteria. It assists in oxidations in which hydrogen is removed from a substance to form water, such as the change from succinic acid,



to fumaric acid,



The reaction goes on in two stages, each needing its own enzyme:



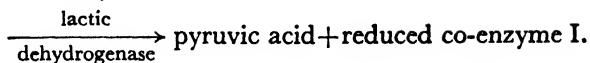
The cytochrome oxidase is the same as the well-known indophenol oxidase. It can be seen from the equations that it is the cytochrome which actually oxidizes the substrate, and that molecular oxygen is only needed for restoration of the cytochrome. This is the justification for the suggestion made above that the restriction of the word 'respiration' to reactions in which oxygen actually takes part is illogical. Cytochrome is responsible for most of the oxidations which go on in animal tissues, and since its oxidation is blocked by cyanide and hydrogen sulphide it is not surprising that these substances are respiratory poisons and reduce oxygen consumption to about 10 per cent. of its normal value.

The mechanism by which lactic acid is oxidized is more complicated. There are three stages, in the first of which hydrogen is removed from lactic acid,



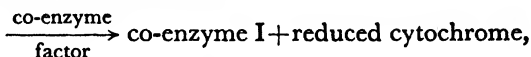
to give pyruvic acid, $\text{CH}_3 \cdot \text{CO} \cdot \text{COOH}$:

lactic acid + co-enzyme I

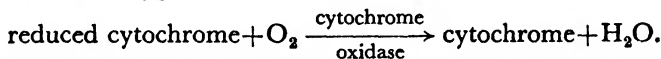


In the second, hydrogen is passed on from reduced co-enzyme I to cytochrome,

reduced co-enzyme I + cytochrome



and the third is the oxidation of reduced cytochrome by molecular oxygen,



Co-enzyme I is a complex substance made up of nicotinamide, adenine, pentoses, and phosphate combined together, and the co-enzyme factor is at present of unknown composition.

Other carriers of importance are the yellow pigment, flavoprotein, which is a compound of a protein with lacto-flavin; glutathione, a sulphur compound; vitamin B_1 ; and possibly ascorbic acid. The first of these chiefly catalyses the oxidation of fats, the second that of some unsaturated fatty acids, and the third that of pyruvic acid. Some oxidizing enzymes are known which work without carriers, such as the one which produces uric acid from other purines. Carbon dioxide is produced by a system in which pyruvate and fumarate jointly react with molecular oxygen giving succinate, which is then restored to fumarate.

Like all chemical reactions, tissue respiration increases rapidly with temperature, as the graph for the oxygen consumption of excised guinea-pig muscle shows (Fig. 13). The curve at first rises rapidly, and corresponds to one calculated on the assumption that an increase of 10°C. multiplies the rate two and a half times. (The ratio

$R_{(t+10)^{\circ}\text{C.}}/R_{t^{\circ}\text{C.}}$ is called the temperature coefficient or Q_{10} .
At 40°C. activity begins to decline, probably owing to

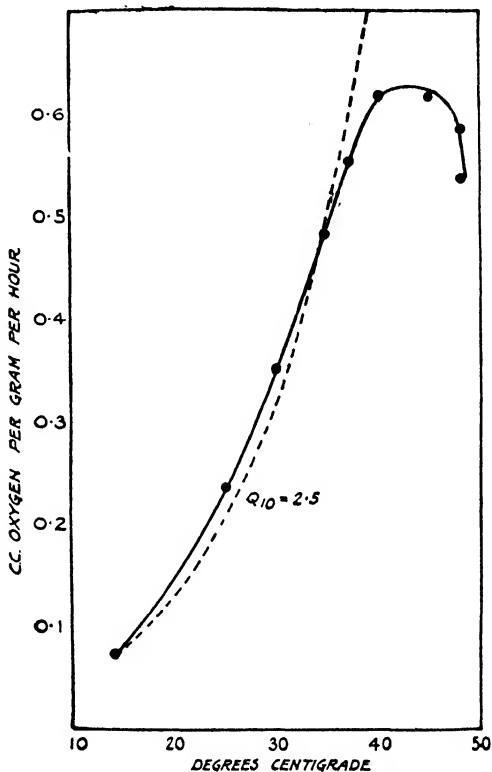


FIG. 13. Effect of alteration of temperature on oxygen usage of plain muscle (guinea-pig uterus).

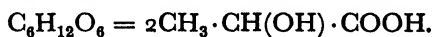
Abcissae = temperature. Ordinates = c.c. oxygen per gm. per hour. The dotted line represents the theoretical curve if the oxygen intake were increased two and a half times for a rise of 10°C. After Starling.

damage to enzymes, and at 48°C. heat paralysis occurs, but the muscle will recover if cooled. Over the lower part of the range the effect does not differ much from that for any ordinary chemical reaction.

3.12. Anaerobiosis

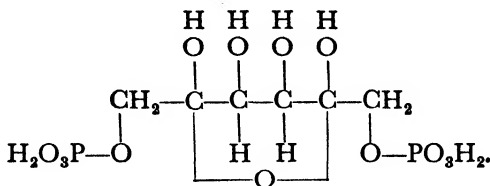
If by anaerobiosis is meant an ability to live completely without oxygen, it is certainly extremely uncommon in animals. It is sometimes said that parasites must be anaerobic, but this is by no means necessarily the case. The cells of the host are supplied with oxygen, and a parasite living in or among them must be able to share it. The only situation in which parasites live where the oxygen concentration is very small is the gut: even here it is probably not zero, for there must be some diffusion out from the wall, which is richly supplied with blood. Considerable attention has been given to *Ascaris*, the common roundworm, for early work suggested that it lived anaerobically by breaking down glycogen to valerianic acid. Later experiments showed that this substance was not formed in sterile cultures, so that its presence was due to bacteria. More recently still it has been shown that *Ascaris* produces carbon dioxide in the complete absence of oxygen, but only to about one-tenth or one-quarter the extent that it does when it is kept in oxygenated Ringer's solution. It is therefore a facultative anaerobe. Other nematodes from the alimentary tract have been shown to be definitely aerobic. It is possible that some parasitic Protozoa, such as *Nyctotherus* in the rectum of the frog, can live anaerobically.

There are many cases where energy is supplied by a reaction in which free oxygen does not take part, the most striking being those included under the heading of glycolysis. The commonest form of this is the break-down of hexose to lactic acid,



This goes on in many vertebrate tissues, and in other animals as well. In vertebrate muscle the reaction is complicated by the intervention of phosphate. The reserve

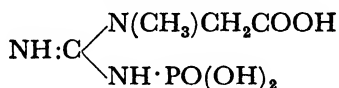
glycogen is broken down by it to hexose, which is then phosphorylated to form fructose diphosphate,



When the fate of this is traced, a number of successive compounds are found to be formed from it. After intermediate changes one molecule of fructose diphosphate gives rise to two molecules of glyceraldehyde phosphoric acid, $\text{H}_2\text{O}_3\text{POCH}_2 \cdot \text{CHOH} \cdot \text{CHO}$, and these, after forming further intermediate compounds, finally form one molecule of each of the acids lactic, phosphoric, and glyceraldehyde phosphoric. The only other substance, apart from catalysts, which takes part in these reactions, is water. The phosphoric acid which has been produced is available for reacting with carbohydrate and going round the cycle again, but it will be noted that one unit of phosphate is still locked up in glyceraldehyde phosphoric acid, and is therefore temporarily lost. It is true that when another hexose molecule has broken down there will be two molecules of glyceraldehyde phosphoric acid, which can react and produce as before one molecule each of lactic, phosphoric, and glyceraldehyde phosphoric acids, but obviously there is some lag in the return of phosphate to the system.

The reactions by which phosphorylation of the carbohydrate is brought about are interesting. There is in muscle a substance called adenylypyrophosphate, which is a nucleotide made up of a purine, a pentose, and three phosphate units. This reacts with carbohydrate, giving to it two molecules of phosphoric acid to form, for instance,

fructose diphosphate. The rest of the nucleotide molecule is left as adenylic acid, which contains only one phosphate group. The adenylypyrophosphate can be resynthesized from adenylic acid and phosphate, but it has just been pointed out that the latter is not liberated fast enough. The extra phosphate to keep the reaction going is supplied by creatine phosphate (called also phosphagen, or phosphocreatine), which acts as a store to supply phosphate when it is required. It has the formula



and breaks down to creatine and phosphoric acid; the latter is then available for reacting with adenylic acid.

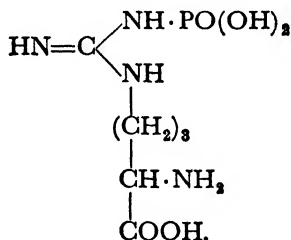
It is unknown at exactly what point in all this the energy for the contraction of the muscle is actually liberated. The break-down of both adenylypyrophosphate and phosphagen liberates energy, and a muscle poisoned with iodoacetate will contract without glycolysis, so it is presumably one of the first two of these three reactions which alone is really necessary for contraction. It is probable that the basic reaction is the break-down of adenylypyrophosphate, and that the break-down of creatine phosphate and later of fructose diphosphate serve to supply energy to restore this. The series of reactions is thus even more complicated than at first appears; adenylypyrophosphate, which might seem to be merely a co-enzyme to facilitate the glycolysis, is also the most important substance present. Glycolysis exists merely to save adenylypyrophosphate, yet the latter must be present to supply phosphate to the carbohydrate for glycolysis to go on at all.

All these reactions are catalysed by enzymes: a myozymase or desmolase which splits the hexose carbon chain; phosphatases, which act at many points in the cycle, and others.

In this series of reactions the anaerobic break-down of glycogen provides energy for the resynthesis of adenylypyrophosphate and phosphagen, the break-down of one of which (probably the former) is all that is actually necessary for a contraction of the muscle. Only small amounts of the phosphorus compounds are therefore required, and contraction can go on until all the glycogen is used up. In the living animal this point is never reached, as the accumulated lactic acid causes fatigue of the nervous system. In man it causes subjective fatigue and pain also, and the good effects of massage after exercise lie mainly in increasing the flow of blood and so distributing the lactic acid over the body.

The break-down of glycogen to lactic acid is a very wasteful method of providing energy, since much remains unused. If oxygen is present an additional reaction takes place, which makes the whole cycle much more efficient. In frog skeletal muscle one-fifth of the lactic acid produced is completely oxidized to carbon dioxide and water, and this provides sufficient energy for the resynthesis of the remaining four-fifths to glycogen. In mammals there is a similar restoration, but it is not certain that the actual resynthesis can go on anywhere but in the liver. This oxidative recovery may continue long after the muscle has done its work, and indeed it normally does so. After half a minute of severe work the oxygen intake in man remains above the normal for a quarter of an hour or more, and after prolonged exercise the lactic acid in the blood may be above the normal for hours. Effectively, then, the energy for contraction is supplied long after this has actually taken place: the animal is said to put up an oxygen debt. This is paid off later, and, since the blood is continually taking lactic acid away from the working organ, the oxidation goes on in other muscles besides those which are contracting. Man rests his legs by not using his arms.

A beginning has been made in finding out how widespread is this means of providing energy. Essentially the same scheme seems to be used in all vertebrate muscles, although the details may be different. Cardiac muscle, for instance, has very little phosphagen, and probably never normally works anaerobically. Since the heart never rests it would be very improvident for it to go into oxygen debt. The chemistry of the electric organs of fishes is also in general similar. In the muscles of nearly all the invertebrates which have been studied a somewhat similar reaction takes place, but creatine phosphate is replaced by a fairly closely related compound called arginine phosphate,



The only invertebrates which possess phosphocreatine are the ctenophore *Pleurobrachia*, the protochordate groups Cephalochordata and Enteropneusta, and the Echinoidea and Ophiuroidea. In the third and fourth of these cases arginine phosphate is present as well. It is interesting that this small piece of biochemistry supports the embryologists' opinion that the echinoderms are more closely related to the chordates than are any other groups of invertebrates. In some active invertebrates very large oxygen debts can be incurred; the bee, for instance, in flight raises its energy production to thirteen thousand times the normal value, whereas in man even in hard exercise the increase is only to twelve times the normal.

Phosphorylating glycolysis is common in other tissues,

such as liver and kidney, and is widespread in the animal kingdom as a whole. There are, however, cases where hexose is split without the intervention of phosphate, the best known being in the brain and in the chick embryo. Cilia and pseudopodia can put up an oxygen debt, but little is known of their chemistry.

It is not surprising that an animal which gets its energy in this way can live for some time without oxygen; earthworms and freshwater snails can survive for six days, arthropods, which are more active, for from two to five hours, and the warm-blooded mammals for a shorter period still. One reason why man can live for only a short time without air is that the nervous system is very sensitive to both lack of oxygen and excess of carbon dioxide. A drowned man who is insensible but not dead cannot revive on restoration to the air unless oxygen is supplied to the body by breathing, and this cannot start until the nerves controlling the respiratory movements receive oxygen. There is therefore a deadlock which can only be resolved by artificial respiration.

It appears that certain tissues may be completely anaerobic. Young chick heart tissue, and certain cancerous cells, can grow *in vitro* completely without oxygen. Cartilage is normally anaerobic within the limits of experimental error, glucose being broken down to lactic acid. Cartilage is without blood-vessels, and possibly the lactic acid diffuses out and is oxidized elsewhere; if this is so it would simply be a special case of the oxygen-debt mechanism.

3.2. Transport of Oxygen

The bigger an animal is, the more oxygen it needs, provided of course that its activity remains the same. Further, if oxygen can make its way in only by diffusion from the surface, the bigger an animal the lower, under given conditions, will be the concentration of oxygen at its centre.

It is obvious that there must be some size at which the concentration becomes too low for activity, and that the animal cannot exceed this size. It is not surprising that all the larger animals have some special means for bringing oxygen to the tissues, although it is impossible to say that such a transport system becomes necessary at a particular size; different animals have different respiratory rates and live in different oxygen concentrations. Isolated frog muscle 4 mm. thick can just live without blood-vessels, and most animals larger than this have some mechanism for oxygen transport. The chief exceptions are the coelenterates, which are either inactive or, as in the Scyphozoa, have a body which is mainly non-living mesogloea. There are two methods of oxygen transport, by tracheae and by a circulatory system.

3.21. Transport by Tracheae

The gaseous oxygen of the air may be carried into the body by tubes called tracheae. These are found in insects, in isopods, in four groups of arachnids (Phalangidae, Pseudoscorpionidae, Solifugae, Araneidae), and in *Peripatus*. It has never been shown that the so-called tracheae of a few coelenterates are respiratory. Those of insects are best known. They arise as ingrowths from the surface, and so are ectodermal however deeply they go in. There is a main longitudinal trunk on each side, which opens to the exterior by spiracles; typically there is on each side one of these between the prothorax and mesothorax, one between the mesothorax and the metathorax, and one on each of the first eight abdominal segments. There are many branches, of which the larger are lined with chitin and the smaller with a protein called trachein. The tracheae end in tracheal cells, from which go out fine intracellular tracheoles (Fig. 14). These in some cases form a capillary network amongst the tissues, and in others

enter individual cells. They are filled with fluid towards their inner end, and the varying osmotic pressure of the cell causes this to be continually moving up and down, which brings oxygen very efficiently into solution (Fig. 15).

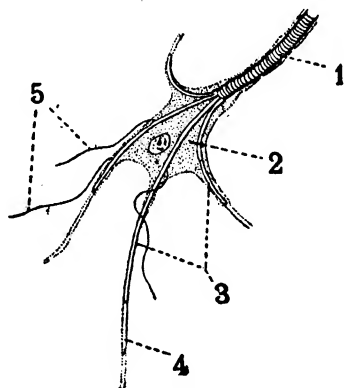


FIG. 14. Detail of tracheal ending.

1, trachea; 2, tracheal cell; 3, main tracheoles containing air; 4, main tracheoles containing liquid; 5, fine tracheoles containing air. After Wigglesworth.

The tracheae of fully aquatic insect larvae (mayflies, dragonflies, stoneflies) have no open spiracles; oxygen is taken up from the water through the thin walls.

3.22. Transport by a Circulatory System

In other cases oxygen is carried round the body in solution. The sea-water in the water-vascular system of echinoderms is respiratory, but in most animals a blood-system not open to the exterior, and containing a special respiratory pigment, is used. A respiratory pigment is a substance which forms a compound with oxygen by means of a reversible reaction, so that it can carry oxygen from regions of high partial pressure of the gas to those where it is low. The fact that this substance is always coloured is accidental. Five groups of such pigments are known; they

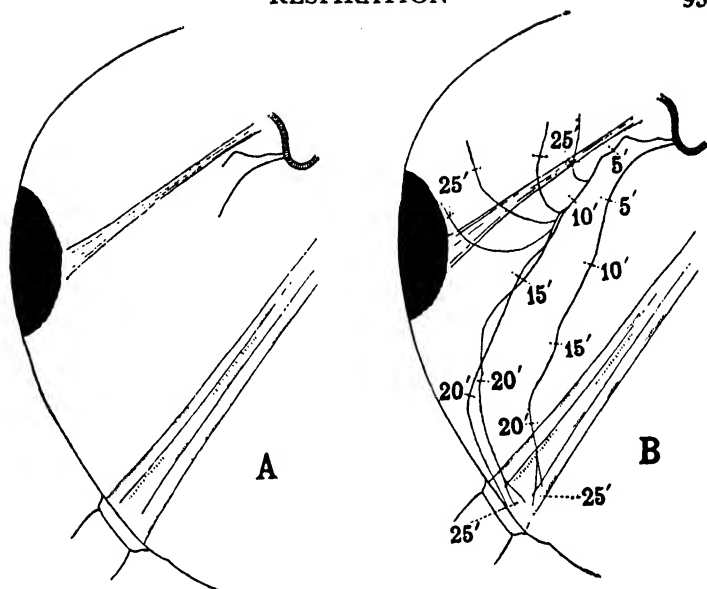


FIG. 15. Effect of asphyxiation on air in tracheoles of a larva of a gnat. A, larva at rest; B, during asphyxiation. The figures in B show time in minutes, after onset of asphyxiation, at which air reached points indicated, so making the tracheoles visible. After Wigglesworth.

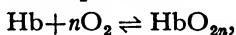
are shown, with some of their chief properties, in Table 1. Haemoglobin consists of a base called protohaem or haematin, which is a ferrous iron porphyrin, united to a

TABLE I
Respiratory Pigments

Pigment	Contained metal	Colour		Occurrence
		Oxygenated	Deoxygenated	
Haemoglobin	Iron	Red	Red	Vertebrates
Erythrocrucorin	Iron	Red	Red	Scattered invertebrates
Chlorocrucorin	Iron	Green	Green	Some polychaetes
Haemerythrin	Iron	Red	Colourless	Some annelids
Haemocyanin	Copper	Blue	Colourless	Most molluscs and arthropods

protein, globin. It is therefore similar to cytochrome, but in the latter the protein part of the molecule is not a globin, and when oxygen is taken up by haemoglobin there is no change in the valency of the iron. The haemoglobins of different species are slightly different in physical properties, and it is probable that the globin differs in different animals. Even the haemoglobin of one species may vary from individual to individual, and that of one individual may be different at different times. The differences are, however, small, and the haemoglobins of species of a genus are usually isomorphic. The red pigment of invertebrates, shown in the table as erythrocrucorin, is usually called haemoglobin, but it differs from the substance in vertebrates in molecular weight, in possessing a base different from, though closely allied to, protohaem, and possibly in other ways. Chlorocruorin, though similar to haemoglobin in fundamental structure, differs from it both in its protein and in the fact that the base, chlorocruorohaem, contains one atom of oxygen more than protohaem.

All these pigments work in the same way, which may be illustrated by haemoglobin. In contact with oxygen this reacts according to the equation



where Hb stands for a molecule of haemoglobin. This is an ordinary reversible reaction, and can be treated by the methods of physical chemistry. Applying the Law of Mass Action, and using the conventional square brackets to represent concentration, we have,

$$k_1[\text{Hb}] \cdot [\text{O}_2]^n = k_2[\text{HbO}_{2n}]$$

$$\text{or} \quad \frac{[\text{Hb}]}{[\text{HbO}_{2n}]} = \frac{1}{[\text{O}_2]^n} \cdot \frac{k_2}{k_1} = \frac{1}{k[\text{O}_2]^n};$$

adding one to each side,

$$\frac{[\text{Hb}]}{[\text{HbO}_{2n}]} + \frac{[\text{HbO}_{2n}]}{[\text{HbO}_{2n}]} = \frac{1}{k[\text{O}_2]^n} + \frac{k[\text{O}_2]^n}{k[\text{O}_2]^n};$$

reversing,

$$\frac{[\text{HbO}_{2n}]}{[\text{Hb}] + [\text{HbO}_{2n}]} = \frac{k[\text{O}_2]^n}{1 + k[\text{O}_2]^n}.$$

Now $[\text{Hb}] + [\text{HbO}_{2n}]$ is a measure of the total haemoglobin present in whatever state it may be, so that this equation gives us a relation between the proportion of the total which is in the form of oxyhaemoglobin, and the concentration of oxygen with which it is in equilibrium. In practice it is convenient to state the oxyhaemoglobin as a percentage of the total, and to measure the oxygen concentration by its partial pressure in millimetres of mercury. The equation must then be modified to read

$$100 \frac{[\text{HbO}_{2n}]}{[\text{Hb}] + [\text{HbO}_{2n}]} = 100 \frac{k(cp)^n}{1 + k(cp)^n},$$

where p is the partial pressure of oxygen and c is a factor relating this to the concentration in gram-molecules per litre.

The form of the curve given by this equation depends on n , the number of molecules of oxygen which combine with one molecule of haemoglobin, and there is an apparent discrepancy here between the calculated curve and those obtained by direct measurement of the haemoglobin. An experimental curve is shown in Fig. 16; it corresponds to a value of n of about 2.5, a figure which can obviously have no physical meaning. The theoretical value of n was determined by ordinary chemical means. Haemoglobin contains iron, and it was fairly easy to find by analysis that 32 gm. of oxygen react with that weight of haemoglobin which contains 56 gm. of iron, so that for each atom of iron one molecule of oxygen is added to make oxyhaemoglobin. The next and more difficult step was to find the molecular weight of haemoglobin, and so the number of atoms of iron in one molecule. Direct measurement of the osmotic pressure of a solution suggested that the molecular weight was about 68,000, and this was

confirmed by measurement of diffusion rates and more precisely by the rate of sedimentation in the Svedberg ultracentrifuge. 68,000 gm. of haemoglobin contain 224 gm.

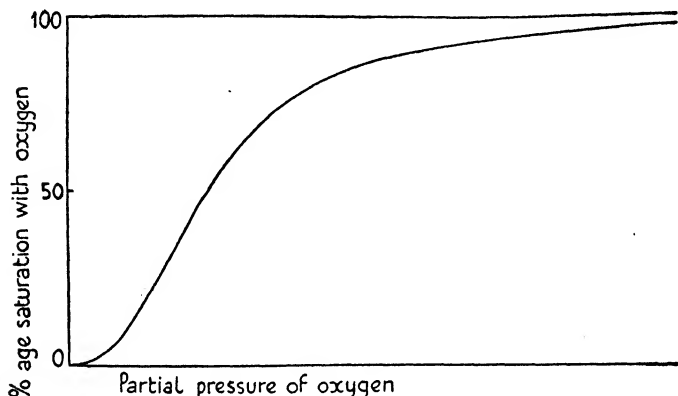
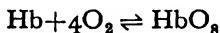


FIG. 16. Dissociation curve of human oxyhaemoglobin under 40 mm. of mercury pressure of carbon dioxide at 38° C. After Haldane.

of iron, so that one molecule contains four atoms of iron and the equation for the reaction with oxygen should be



and $n = 4$.

The discrepancy cannot be explained without taking into account two other facts. When an experimental dissociation curve is plotted either for a concentrated solution of haemoglobin or for one which is entirely free from the ions normally present in blood-plasma, it is found to be a rectangular hyperbola, for which $n = 1$. This could be easily explained on the assumption that although the gross equation for the oxygenation of haemoglobin involves four molecules of oxygen, these are in fact added on one at a time to make intermediate compounds which have only a transitory existence. There are indeed good reasons for thinking that reactions involving five molecules very sel-

dom take place, owing to the small probability of so many being in collision at once. One more assumption, for which there is some evidence, will bring the ordinary curve into

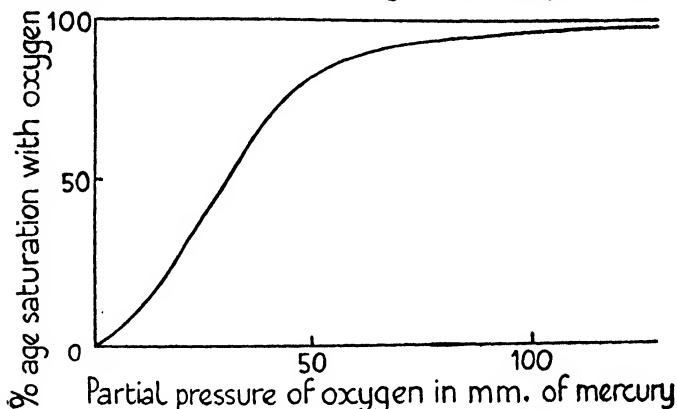


FIG. 17. Theoretical oxyhaemoglobin dissociation curve. See text, and cf. Fig. 16.

line. Both haemoglobin and oxyhaemoglobin are acids, and as such react with base whenever it is present. In the normal conditions in which they occur, that is in blood, carbonic acid is present as well, and there is not sufficient base present to saturate both this and the haemoglobin, so that an equilibrium is reached which depends on the relative affinities of the base for the different acids present. Now oxyhaemoglobin is a stronger acid than haemoglobin, so that when blood takes up oxygen a new equilibrium is set up and some of the base which was formerly held by carbonic acid is transferred to oxyhaemoglobin. If the further assumption be made that as haemoglobin (or oxyhaemoglobin) takes up base its affinity for oxygen (k , above) increases, the problem is solved, except in small detail. Fig. 17 shows one of many curves which can be constructed on this basis; it is obviously very similar to Fig. 16. When no base is present, or when there is excess

so that the haemoglobin is saturated, k cannot alter and the dissociation curve is a normal rectangular hyperbola, as it is found in practice to be.

Whatever be the exact details of the theory, there is no doubt of the validity of the general equation derived above, and it is the practical consequences of this which make it possible for haemoglobin to act as an oxygen-carrier: for the equation means that a given partial pressure of oxygen is in equilibrium with only one definite percentage of oxyhaemoglobin. If, therefore, haemoglobin is brought into a high pressure of oxygen, as it is in the lungs, and then taken to a low pressure, as happens when it is taken by the circulatory system to the tissues, it must take up oxygen in the former place and give it up in the latter. There is no need for vague talk of loose compounds, for the whole matter can be explained in terms of ordinary physical chemistry. The actual position of the curve depends on k , and this varies with the particular haemoglobin used: it can further be altered by other factors in the environment. It is the ratio of the two velocity constants k_1 and k_2 , and so will be altered by anything which alters these to different extents. The effect of two important physical factors can be forecast by the application of the principle of Le Chatelier. The reaction $\text{Hb} + 4\text{O}_2 = \text{HbO}_8$ is exothermic. Hence a rise in temperature shifts the equilibrium point of the reaction to the left, k_2 is increased more than k_1 so that k is lowered, and the curve as a whole moves to the right (i.e. a given partial pressure of oxygen is in equilibrium with a lower percentage of oxyhaemoglobin). Oxyhaemoglobin is a stronger acid than haemoglobin, so that an increased hydrogen-ion concentration acts in exactly the same way as a rise in temperature, and dissociates oxyhaemoglobin. This is important in the animal's tissues, because where an organ is active and more oxygen is therefore required,

there is usually much lactic acid and carbon dioxide, and so a high acidity. Oxyhaemoglobin therefore dissociates most readily when it is most needed.

Similar curves are given by all the other pigments, but they are not all affected in the same way by physical factors.

Oxygenated blood is nearly fully saturated, and venous blood is about half saturated, and it is therefore over this range that the blood works. The pressure of oxygen in equilibrium with blood containing 95 per cent. of its pigment in the oxygenated form, is called the loading tension (t_L), and that in equilibrium with 50 per cent. saturated blood the unloading tension (t_U). A statement of these shows the condition under which the blood will work efficiently. Table 2 shows that the more active

TABLE 2

Loading and Unloading Tensions of Bloods. (Various authors)

<i>Animal</i>	<i>Pigment</i>	<i>Temperature</i> °C.	t_U mm. Hg	t_L mm. Hg
Mammals . . .	Haemoglobin	38	c. 27	c. 90
Sea-fish and trout . .	"	17	12-15	30-40
Carp, pike . . .	"	15	2-3	10
<i>Planorbis</i> . . .	Erythrocrucorin	12	1-2	15
<i>Arenicola</i> . . .	"	20	1.7	5
<i>Spirographis</i> . . .	Chlorocrucorin	10 (pH 8)	9	c. 26
" . . .	"	26 (pH 7.35)	29	c. 50
Crustacea . . .	Haemocyanin	15	14	33
<i>Helix</i> . . .	"	11	4	17

animals, and those which live in regions of high oxygen concentrations, have higher values for these functions. This allows for the best possible use of the oxygen supply, for it means that the blood starts to give up its oxygen when the tension in the tissues is only a little below that of the atmosphere. The blood of *Arenicola*, with a

loading tension of 5 mm., only starts to provide oxygen at a partial pressure at which mammalian haemoglobin is almost completely dissociated. The worm lives for part of its time under conditions of low oxygen tension, and if its pigment had a high loading tension it would be unable to supply oxygen when it was most needed.

In the living animal there is a gradient of oxygen tension from the atmosphere to the blood-plasma, from the plasma to the pigment, from the pigment back again to the plasma in the capillaries, and from the plasma to the active tissues. Oxygen necessarily follows this gradient, the pigment combining with oxygen at the surface, and dissociating in the interior of the body. Muscle haemoglobin, with a different chemical composition, and with a hyperbolic dissociation curve mostly to the left of that for blood haemoglobin, is present in mammals, and acts as the final link by which oxygen is taken to the tissues (Fig. 18). It also serves as a short-time oxygen store.

The carrying power, that is the amount of oxygen which a given volume of blood will carry, is quite independent of the dissociation curve. Some typical values are shown in Table 3. It is noteworthy that in vertebrates, where the pigment is contained in corpuscles, the carrying power is very high. One advantage of the corpuscles is that their

TABLE 3
Carrying Power of Bloods. (Various authors)

<i>Fluid</i>	<i>Pigment</i>	<i>Per cent. oxygen by volume when saturated</i>
Sea-water . . .		0.7
Human blood . . .	Haemoglobin	19.0
<i>Arenicola</i> blood . . .	Erythrocrucorin	5.7
<i>Spirographis</i> blood . . .	Chlorocrucorin	9.1
<i>Cancer</i> blood . . .	Haemocyanin	1.6
<i>Octopus</i> blood . . .	„	4.7

walls are impermeable to the pigment, so that this can be present in high concentration. If it were free in the blood to anything like the same extent, it would inevitably be lost through the kidneys.

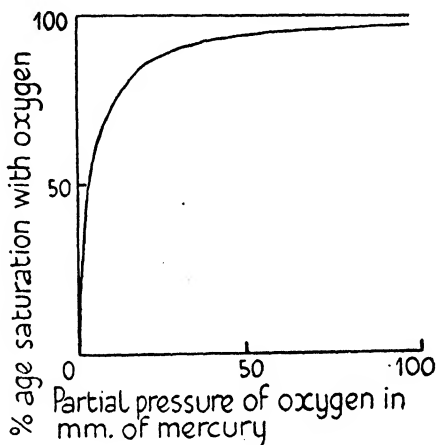


FIG. 18. Dissociation curve of muscle oxyhaemoglobin. Cf. Fig. 16. After R. Hill.

Invertebrate haemoglobin (erythrocrucorin) is capable of working only at very low oxygen tensions. In *Planorbis* and some others it acts only as a reserve form of respiration under bad conditions, for under normal circumstances it is never dissociated. It is possible that in *Arenicola* it functions as an oxygen store, giving up the gas when the worm is cut off from fresh supplies when the tide is out. One experimenter concluded that it contains enough oxygen to last for three hours, which is the normal time for which the animal is not covered by water, but another decided that it would only last for thirty minutes. In any case it is probable that it does hold oxygen which is available during anaerobic conditions.

There is some connexion between the rate of supply

of blood and the requirements of the animal for oxygen. In vertebrates the heart has a double innervation, from the depressor branch of the vagus, and from the sympathetic system. Impulses are continually passing down the former, antagonizing the effect of the latter and preventing the heart from racing. In mammals the sympathetic is stimulated and the heart-beat raised both by low external temperatures and by decreased oxygen tension. In cold-blooded animals such as the frog, *Daphnia*, and the unhatched chick, raising the temperature increases the heart-rate.

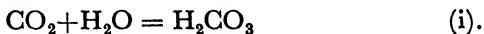
In passing, it may be mentioned that haemoglobin, chlorocruorin, and haemocyanin form compounds with carbon monoxide. In the case of the first two the action is reversible, but it is nearly complete at very low concentrations of the gas, and the velocity constant for the dissociation is very low. Consequently carbon monoxide is poisonous to animals with either of these pigments. It can be shown by consideration of the reaction between haemoglobin and oxygen and carbon monoxide, when these gases are present together, that a high percentage of oxyhaemoglobin can be formed only if the oxygen concentration is very high. This agrees with the standard method of treating carbon monoxide poisoning, which frequently occurs after coal-mine explosions. The patient is given a mixture of 93 per cent. oxygen and 7 per cent. carbon dioxide; the function of the latter is to raise the heart and respiratory rate.

3.3. Transport of Carbon Dioxide

Strictly speaking, the removal of carbon dioxide is a matter of excretion, but it is closely connected with the transport of oxygen, and it is one of the functions of respiration in the narrow sense, so that it will be dealt with here. Some carbon dioxide undoubtedly finds its

way out of the animal by simple diffusion, especially since it can diffuse through vertebrate connective tissue thirty times as fast as does oxygen, and since chitin is fairly permeable to it. Where there is a blood system this seems always to be used as well, and while the following account applies in details to mammals, fishes and reptiles are similar.

Carbon dioxide dissolves in the plasma in the ordinary way and there combines with water to form carbonic acid:



This reaction is catalysed by the enzyme carbonic anhydrase. It goes on also inside the red corpuscles, and in these the acid reacts with haemoglobin, most of which is present as the potassium salt:



The chief ions that are present are therefore

in the plasma Na^+ and Cl^- ,
in the corpuscles K^+ , HCO_3^- , H^+ , and Hb^+ .

The walls of the corpuscles are permeable to anions, but not to cations nor to the large haemoglobin ion. Under these circumstances the chloride ions diffuse in and the bicarbonate ions out, to give what is called a Donnan equilibrium, from the name of the chemist who investigated it. The result is that carbon dioxide is carried as sodium bicarbonate in the plasma, and that much more of the gas can be taken up than by mere physical solution or formation of carbonic acid. When the pressure of carbon dioxide is reduced the reaction is reversed; the corpuscles act like an acid in dissociating the bicarbonate. Oxyhaemoglobin is a stronger acid than the reduced form, and so when it is present reaction ii does not go so far and less carbon dioxide can be carried; hence oxygen, by forming oxyhaemoglobin, displaces carbon dioxide from the blood.

There are subsidiary phenomena, of which the following are the chief.

In the plasma, carbonic acid decomposes the sodium salts of the proteins present,



In the corpuscles, potassium phosphate is similarly decomposed,



Reactions iii and iv together carry about 5 per cent. of the carbon dioxide. Lastly, carbon dioxide combines directly with haemoglobin,



and this accounts for 30 per cent. of the total amount present in the blood.

3.4. Respiratory Organs

The mere possession of a respiratory pigment is not by itself enough to ensure an adequate supply of oxygen to the tissues. There must be some part of the body where oxygen can combine with the pigment. The simplest way is for the animal to make use of its skin, a method used by many small aquatic animals and by those living in damp and protected situations. Examples are numerous. Earthworms obtain all their oxygen through the unspecialized body-surface, and even in polychaetes with well-developed gills 75 per cent. of the gas exchange may take place through the skin. A few Crustacea, such as *Coenobita*, the semi-terrestrial hermit crab which feeds on coco-nuts, have no gills, and there are some Apterygota without tracheae, and a few aquatic insect larvae (*Simulium*, *Chironomus*) where they are not functional; but for the most part arthropods have some specialized system. The same applies to the molluscs. There are a few scat-

tered cases of fish which breathe through the skin; the mudhopper *Periophthalmus* of the East Indies uses its caudal fin when it is on land, and the eel uses its whole body-surface when it is migrating across country. In the Amphibia the skin is very important. Some Salamandridae have neither gills nor lungs, and the axolotl is not affected by having both cut off. In the edible frog one-third of the total oxygen exchange, and three-quarters of the carbon dioxide exchange, go on through the skin. The amniotes have too thick a covering of scales or fur or feathers for the skin to be used very much, but even in the cat 0.5 per cent. of the gas exchange goes on through it.

The oxygen requirement of an animal depends on its volume, and the rate at which its skin can take up the gas depends on its surface. The larger an animal is the smaller is the ratio of its surface to its volume, so that there is likely to be some size at which the skin is not capable of taking up oxygen fast enough. This point will be reached early when the animal has a poor circulation, or is very active, or has a thick epidermis. Thus the largest animals which use nothing but the unspecialized skin to take up oxygen are the six-foot-long earthworms of the East, which are sluggish, have no exoskeleton, and have a closed blood system with haemoglobin of low loading tension. Fish, which have thick scales, can seldom use their skin, whereas the naked Amphibia, as has been said, in some cases use nothing else.

Where the skin is not adequate some special respiratory organ, usually highly vascular, is developed, either from the skin or some other part of the body. If it is used for absorbing the dissolved oxygen of water it is generally called a gill; if it works in air, a lung. From a physiological point of view an organ is not a gill unless it takes up oxygen at a greater rate per unit area than does the rest of the body-surface, and judged in this way many of the structures

which morphologists call gills do not deserve the name. The gills of lamellibranchs, for example, are feeding organs, the true respiratory organ being the mantle, and the anal gills of mosquito and midge larvae are organs for water exchange. Good examples of external gills, that is those which are expansions of the skin, are found in the marine gastropods and in Crustacea such as the crayfish. In vertebrates they occur in a few fishes such as *Polypterus*, and fairly widely in the Amphibia; in all these cases they are probably adaptations to bad oxygen conditions.

The aquatic larvae of Trichoptera, Ephemeroptera, Odonata, and *Simulium* (Diptera) have tracheal gills, expansions of the body wall with a network of fine tracheae, but these do not always absorb oxygen.

A good many animals make use of the alimentary canal instead of the skin. Some polychaetes and aquatic oligochaetes (e.g. *Nais*, common in British waters) have an ascending ciliary current beginning at the anus, often assisted by antiperistalsis, and the rectum is similarly used by many primitive Crustacea such as the water-fleas, and even to some extent by the crayfish. Dragonflies of the sub-order Anisoptera have rectal tracheal gills, similar except in position to those of other aquatic larvae. The Holothuroidea breathe by respiratory trees, which are branched diverticula of the cloaca. The most notable examples, however, are the vertebrates. In addition to peculiar cases such as some tortoises which pump water in and out of the cloaca, there are the internal gills of fish, which are expansions of the pharynx wall, and the lungs of tetrapods, which are outgrowths from the same region. A few fish (the Dipnoi, Crossopterygii, and Holostei, represented by *Ceratodus*, *Polypterus*, and *Amia* respectively) use the swim-bladder, which is simply a lung which in most cases has become adapted to other uses, and the frog largely uses the roof of its mouth.

3.41. Breathing

In inactive animals such as the earthworm there is no special arrangement for bringing oxygen to the respiratory surface, but most species have something of this sort, particularly when the respiratory organ is internal. Constant renewal of the layer of air or water immediately in contact with the absorbing surface effectively increases the supply of oxygen, for if the gas can only arrive by diffusion its concentration in the atmosphere immediately adjacent to the surface will rapidly fall to a low value. The polychaetes *Spirographis spallanzanii* and *Sabella pavonina* live in tubes through which they maintain a current of water by rhythmical contractions of the body; a swelling appears at the hind end of the worm, completely filling the tube, and then moves forwards. The result of this is that the worms can live in the tubes in water of low oxygen concentration, while if they are removed from the tubes they can only survive if the water is well aerated. That no special property of the tubes is involved is shown by the fact that the worms can live in low oxygen concentrations if they are in glass tubes. Presumably the waves of muscular contraction are stimulated by contact with the tube.

The beating of the heart in *Daphnia* prevents water from remaining stationary under the carapace, and in most of the higher Crustacea some of the limbs maintain definite currents over the gills. In the decapods, such as the crayfish and shore-crab, the exopodite of the second maxilla is modified as the scaphognathite, which flaps and draws water forwards through the gill chamber about once a second. Other mouth-parts assist in the process, some of them ensuring that the current actually passes over the gills, and the epipodites of the three maxillipedes brush the surfaces of the gills to prevent the accumulation of foreign matter. The scaphognathite reverses for a few strokes every now and again. The effects of oxygen and

carbon dioxide concentration on the beat of the respiratory limbs of several Crustacea has recently been investigated. They fall into three groups: in the first, represented by the shore-crab (*Carcinus moenas*), the beat is independent of the concentration of the two gases. In the second, of which the amphipods *Gammarus pulex* and *G. locusta* are examples, the beat (in this case of the pleopods) is increased by falling oxygen tension and by increasing carbon dioxide tension. In the third, typified by the crayfish (*Potamobius astacus*), the beat is increased by oxygen deficiency but is unaffected by carbon dioxide. The distribution of these three groups certainly does not follow the classification of the Crustacea, and neither does it seem to agree with the habitats or habits of the animals. It appears that the power to regulate the respiratory current in accordance with needs has been independently evolved on several occasions.

In the lamellibranchs the ciliary food currents (see p. 9) also serve to bring in oxygen. Pulmonates renew the air in their lung at fairly frequent intervals, since all the gas is expelled when the animal contracts into its shell. The freshwater forms, such as *Planorbis* and *Limnaea*, frequently come to the surface, push the pulmonary aperture into the air, open it, raise the floor of the mantle cavity, and lower it again. This brings in fresh air.

In the selachians each gill pouch is divided into two parts: an inner chamber which is in free communication with the mouth, and an outer which opens to the sea by the externally visible gill slit. These two are separated from one another by the lattice-work of the two hemibranchs. Water passes through the gaps in the lattice by two mechanisms. In the first, which is of the nature of a force pump, the hypobranchial musculature contracts and lowers the floor of the pharynx, so that water enters through the mouth and spiracles, the external openings

of the gill slits being shut. The mouth and spiracles then close, and adductor muscles contract and draw the epi- and cerato-branchials nearer together; the increased pressure in the pharynx forces water through the lattice of the gills into the outer chambers of the gill pouches, and so to the exterior. In the second mechanism, which is a suction pump, the outer gill chambers are first enlarged by the contraction of the adductor muscles and of muscles in the gill septum. While this is happening the external openings of the gill slits are closed, so that water must be drawn through the gills from the inner gill chambers. The outer gill chambers are emptied to the exterior by the contraction of superficial muscles, back-flow into the inner chambers being prevented by the high resistance of the small channels in the gills. By this method breathing can take place with the mouth continuously open. The two mechanisms may work in conjunction with one another, or independently. In teleosts the same methods are used but here there is a single outer gill chamber on each side, the operculum covering all the gills.

The breathing of the frog, apart from the use of the skin mentioned above, does not seem to be very clear. In the ordinary way air is continually being pumped into and out of the buccal cavity through the nares by the movement of the floor of the mouth by muscles attached to the hyoid. The mouth and the glottis are kept closed. About once a minute the external nares are closed, the glottis opens, and the collapse of the elastic lungs forces the air contained in them into the mouth; it mixes with fresh air there, the floor of the mouth is raised, and so the lungs are refilled. If a frog which has recently been active be watched, it can be seen that the thorax pulsates at the same rate as the floor of the mouth, but slightly out of phase with it, so that the lungs are presumably filled more frequently. One thing that is certain is that if the mouth

is held open the thorax ceases to pulsate and the animal shows signs of distress.

In mammals the process of breathing is a complicated one, but an outline of what happens in man is as follows. In inspiration the diaphragm, which is convex upwards, is contracted; the ribs, normally directed forwards and slightly downwards, are raised; and there is a slight extension of the spinal column. All these movements increase the volume of the thoracic cavity, and so reduce the pressure in it. Atmospheric pressure, therefore, forces air into the lungs, which expand to take up the increased volume of the thorax. If the thoracic wall is punctured, breathing is impossible, for air merely rushes in through the perforation. Expiration is the reverse of inspiration, but it is mainly carried out passively. The lungs are elastic and contract of their own accord as soon as the muscles of the diaphragm and ribs are relaxed. The lungs are never completely emptied, so that the oxygen tension in the alveoli is never equal to that of the atmosphere. It is normally about 107 mm. of mercury, about two-thirds that of the air. The respiratory movements are controlled by the central nervous system from the medulla. An increased acidity or decreased oxygen content of the blood reaching the brain causes an increased rate of breathing. In life the chief control is by the carbon dioxide content of the blood, acting through the hydrogen-ion concentration, and in extreme cases the lactic acid formed by glycogen break-down is effective. Since both these substances are formed when a muscle contracts, it is obvious that exercise should cause an acceleration of breathing, and it is familiar to every one that it does in fact do so. Under ordinary circumstances the oxygen content of the blood does not vary significantly, but in cases of difficult breathing or at high altitudes it may fall sufficiently to have an effect. Rapid breathing, and the

other symptoms of mountain sickness, only become noticeable at rest at heights above about 14,000 ft., and under these conditions the tension of oxygen in the alveoli of the lungs is only just above half the normal.

In birds breathing is very efficient; air is taken right through the lungs to the air-sacs, and is then forcibly expelled through the alveoli of the lungs. The oxygen tension in contact with the blood is therefore that of the atmosphere.

The replacement of air in the tracheae of insects is surprisingly rapid; if a cockroach is kept in pure oxygen till its tracheae are full of this gas, and then returned to air, it is only a minute before there is 80 per cent. of nitrogen in them. In most insects diffusion is assisted by some sort of pulsation of the abdomen, assisted during flight by movements of the wing muscles. It has been claimed that in grasshoppers a current of air is maintained right through the body, in at the anterior spiracles and out posteriorly, but the experiments involve very unnatural conditions and the conclusion is doubtful. It has been shown that insects suffer easily from water loss, and in most of them at rest the spiracles are closed, presumably to prevent this. When the rat-flea *Xenopsylla cheopis* is at rest, its spiracles open and close rhythmically, but when the muscles are active they remain open. Experimentally they can be induced to do so either by low oxygen concentration or high carbon dioxide concentration.

Those insects which, like mosquito larvae and many of the beetles, live beneath the surface of water but come to the air to breathe, are of some interest. The opening of the tracheae is covered with hydrofuge substances. These have a high angle of contact with water, which is thus prevented from entering, but oil will wet them, so that a film of it spread on the surface will enter as soon as the spiracles touch it. Once the tracheae contain oil no air

can go in and so the animal must drown. Many insects (such as *Dytiscus* and *Notonecta*) carry bubbles of air below the surface with them. This is used directly as a source of oxygen, and it also enables them to extract oxygen from the water in the following way. Oxygen is being used by the animal, so that its partial pressure in the bubble falls, and in time goes below that in the water. But as this happens the partial pressure of the nitrogen in the bubble must necessarily rise and will go above that in the water, for the total pressure in the bubble is determined simply by its depth below the water, and is constant. Equilibrium can be restored either by oxygen entering the bubble or by nitrogen leaving it, but the first goes on three times as fast as the second, so that very little of the latter takes place. *Notonecta* was found to be able to live for seven hours below water saturated with air, but only thirty-five minutes below water saturated with oxygen. In the latter case the nitrogen in the bubble would rapidly dissolve in the water, and the conditions described above would not apply, so that although as much oxygen was present as in the first case, it was not available.

3.42. Comparison of Aquatic and Aerial Respiration

The question is sometimes asked whether aquatic or aerial respiration is the more efficient. The question is probably meaningless, since the conditions which have to be fulfilled are very different for the two. It has been suggested that since the teleost *Erythrinus unitaeniatus*, which can breathe completely through either gills or lungs, has a slightly greater area of the latter, aerial respiration is less efficient, but obviously no conclusions can be drawn unless full information is available as to the activity of the fish. Nevertheless, there is some reason for saying that air-breathing is less efficient. Ultimately all respiration

is aquatic, since the first thing the oxygen has to do when it reaches the surface of the lung is to dissolve in the surface film of water. The difference between lungs and gills from a physiological point of view is that the former are covered with a relatively thick surface film of water, while the latter may be swept by a current so that the stationary layer is only a few molecules thick. Although there is more oxygen in the air than in water, it is not so easy for the animal to obtain it. The four species of snail *Littorina littorea*, *L. obtusata*, *L. rudis*, and *L. neritoides* form an ecological series of animals which live in progressively drier situations on the shore. The first lives in rock pools and is only exposed at low tides, but the others may be exposed for several hours. Associated with the habitats is the degree of vascularization of the mantle cavity, which increases in the same order as the dryness of the surroundings.

The rate of diffusion of oxygen in air is 45,000 times that in water, so that unless there were some means for continual renewal of the layer of water in contact with the gill, access of oxygen would be much slower than in air.

Land animals drown largely because their lungs become covered with mucus which prevents free access of oxygen. Earthworms can live under well-aerated water. If what has been said above is correct, there seems no reason why aquatic animals should not be able to live in air; that they cannot is probably due to other causes, and in fish the important factor is the haemoglobin. The effective concentration of carbon dioxide in water is not altered by respiration, owing to the presence of bicarbonates. It does not therefore matter that a fish's haemoglobin is very sensitive to carbon dioxide, or, rather, to acidity. In some cases the loading tension in presence of 2 per cent. carbon dioxide is 150 mm. of mercury. In air, respiration very greatly raises the carbon dioxide concentration—there is

5 per cent. in the lungs of mammals—so that if the concentration near the gills rises to anything like the same extent, as it probably does when a fish is brought into air, it is not surprising that the animal dies. It is noticeable that many of those fish which do live on land breathe, like the eel, through the skin, so that carbon dioxide is easily carried away.

IV

EFFECTOR SYSTEMS

EFFECTOR systems are cells, collections of cells, or parts of cells (using the word in its old and broad sense) by which the organism acts in some way on the environment outside it, and it is by means of them only that an animal can respond to a stimulus or produce any change in its own position or in its own body. Put briefly, in the words of G. H. Parker: 'Effectors are the parts by which animals respond to changes in the world about them.' They are usually classified as follows:

1. Cilia and flagella.
2. Pseudopodia.
3. Muscles.
4. Glands.
5. Electric organs (a specialization of 3).
6. Luminescent organs (a specialization of 4).
7. Nematocysts or urticators.
8. Chromatophores.

In addition, there are some minor types, such as the trichocysts and myonemes of some Protozoa. No animal has all of these, and most possess but three of four. Man, for instance, has only pseudopodia, cilia, glands, and muscles, and of these the last alone have any important connexion with the outside world; all the rest serve only to maintain life inside the animal. Effectors are usually brought into action by stimulation either through the nervous system or by hormones, but there are cases of all classes, except electric organs, where the effector apparently reacts directly to a stimulus. Such an organ is called an independent effector, but its nature and reaction are not affected by the method by which it is activated.

4.1. Cilia and Flagella

Cilia and flagella are contractile outgrowths from a cell, never withdrawn except at reproduction and encystment, and maintaining a shape and size which are nearly constant. Although it is usually easy to decide whether a given structure is a cilium or a flagellum, there are some cases of difficulty. Most cells which have contractile processes which conform to the above description have either a few long ones or many short ones, the former being called flagella and the latter cilia. The doubt arises with animals such as the protozoans *Multicilia* and *Trichonympha*, which have many long processes. It is probable that physiologically these are flagella rather than cilia. In any case the two are probably fundamentally very similar, and the differences may be largely due to necessary mechanical dissimilarities between a short structure and a long. Flagella are found in the Protozoa, in sponges, in some of the endoderm cells of coelenterates, and in the sperms of most animals. Cilia are even more widespread: they form the locomotor organs of a whole class of the Protozoa, of ctenophores, of some planarians, and of rotifers, and of larvae of coelenterates, platyhelminths, annelids, molluscs, echinoderms, protochordates, and of Amphibia. Internal ciliated cells are present in all Metazoa except Nematoda and Arthropoda; they serve to maintain currents of water for many purposes: for carrying food (Scyphozoa, lamellibranchs, protochordates), for carrying out excretory products (all groups with a true nephridium; see p. 60), for carrying eggs (vertebrates), or for guiding sperms to the eggs (birds and reptiles). In the mammals cilia are present chiefly in the respiratory tract, where they help to keep out dust particles. They are found in all three germ-layers, and wherever they occur are very similar in structure and behaviour.

Both cilia and flagella are very thin structures, and in nearly all cases they appear homogeneous under the microscope. A few large flagella have been described as showing an axial filament when fixed, but it is doubtful whether this has any real existence. Some large cilia, such as the laterofrontals of *Mytilus* (see p. 8), have been shown to consist of several cilia beating together so that unless their co-ordination is upset they appear as one. In a similar way many undulating membranes consist of a line of cilia beating in order. When the rhythm is upset by placing a needle through the apparent membrane, the individual cilia can be seen. There are some authors who consider that all undulating membranes, even that of *Trypanosoma*, are of this nature.

In a preserved cell it is usually possible to see at the base of a flagellum a basal granule, and below the cilia a line of granules, presumably one for each cilium. In living cells of ciliated epithelium there is sometimes a region of slightly higher refractive index corresponding in position to the basal granules. In some fixed cells fibres called rhizoplasts run from the basal granules to the nucleus, and where the granules are remote from the surface there may be an axial filament running from each granule to its flagellum. This is particularly well seen in some of the complicated Mastigophora, such as *Giardia* (Fig. 19). In some cases it has been possible to peel off the surface layer of cells of ciliated epithelium, and when this has been done it is found that if the basal granules come away with the cilia the latter go on beating normally, but if the region with the granules is left attached to the main part of the cell the cilia are inactive (Fig. 20). These observations suggest that the basal granules are necessary for the functioning of the cilia. A basal granule seems always to be derived from a division centre, but nothing appears to be known as to the way in which it acts.

The rate of movement of cilia appears high, but this is because, while velocity has dimensions of one in length and minus one in time, the microscope magnifies length

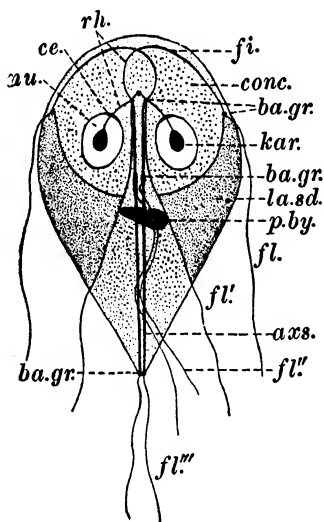


FIG. 19. *Giardia intestinalis*, from the intestine of man. Semi-diagrammatic.

axs., axostyle (axoneme); *ba.gr.*, basal granules; *ce.*, centriole; *conc.*, ventral concavity ('sucker'); *fi.*, fibre around concavity; *fl.*, *fl'*, *fl''*, *fl'''*, anterolateral, posterolateral, ventral, and caudal flagella; *kar.*, karyosome; *la.sd.*, lateral shield, the thickest part of the body; *mu.*, nucleus; *p.by.*, parabasal body; *rh.*, rhizoplasts. After Borradale and Potts.

but leaves time unaffected; it therefore magnifies velocity to the same extent as it does length. A cilium 10μ long, beating at the normal rate of ten times a second and moving through an arc of π radians, has in its effective beat a velocity of only 1.5 mm. per sec. at the tip. The speeds produced by cilia correspond to this; *Paramecium* moves at speeds of the order of 1 mm./sec., and particles placed on ciliated epithelium never move at more than 3 or 4 mm./sec. *Euglena* moves at about 0.2 mm./sec. On account of their slow speed, and because they can only be present on surfaces, which bear a progressively smaller proportion to weight as size increases, cilia can only be used for efficient locomotion if the animal is

small and of low density. Thus *Volvox*, with a radius of 0.5 mm. and a specific gravity of 1.01, has a maximum velocity at 15° C. of 1 mm./sec. At this speed practically all the external work is done against viscosity, and if all the cilia were to stop beating at once the kinetic energy of the animal would only carry it 0.05 mm.—one-tenth of its own radius. In the same way full speed is attained almost at once.

The movement of cilia can be studied in three ways: they may be slowed down with drugs such as veratrin; they may be observed with a stroboscope; or they may be photographed with a kinecamera. It is obviously of doubtful legitimacy to argue from a drugged cilium to the

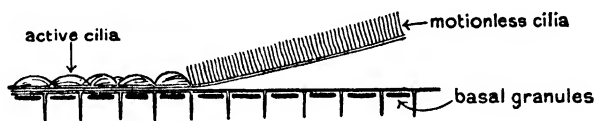


FIG. 20. Excised strip of lateral epithelium of *Mytilus* (diagrammatic). Note that the cilia are active as long as they are in organic communication with the cells. After Gray.

normal, so that the first method, though useful, must be supported by others. The principle of the stroboscope is as follows. If a moving object is seen through a rapidly opening and closing diaphragm, it is observed in the positions which it occupies at times 0 , δt , $2\delta t$, $3\delta t$, and so on, where δt is the interval between successive openings of the shutter. If δt is small enough the eye, owing to persistence of the retinal images, will appear to see continuous movement. If the object is not moving laterally, but is going through a cyclic movement like that of a rotating wheel, and if it takes a time t for one complete cycle, it is in the same position at $t+\delta t$ as it was at δt , the same at $t+2\delta t$ as at $2\delta t$, and more generally in the same position at $t+m\delta t$ as at $m\delta t$. For successive revolutions the same argument holds, and the wheel is in the same position at $2t+m\delta t$ as at $m\delta t$, and more generally in the same position at $nt+m\delta t$ as at $m\delta t$ (where n is a whole number). If, then, the diaphragm is arranged to open at intervals of $t+\delta t$, the object will be seen at times 0 , $t+\delta t$, $2t+2\delta t$, and so on. It will therefore be observed in exactly the positions that it would have occupied at times 0 , δt , $2\delta t$, &c., and so will appear to be in continuous movement at much less than its normal speed: how much less

will depend on the relative values of t and δt . For investigating ciliary movement the cilium is viewed through a slit in a rotating disk, the rate of revolution of which is adjusted so that the cilium appears to stand still: at this speed the disk rotates once while the cilium goes through one or possibly more exact cycles. The speed of the disk is decreased slightly and the conditions discussed above become operative. The cilium is seen to move slowly. The speed of the disk must be such as to avoid flicker.

The third method consists simply in combining a kine-matograph camera with a microscope. It is sometimes convenient to add a stroboscope to this arrangement.

All the methods of investigation agree in showing that the method of beat is that shown in Fig. 21 and Pl. II. There is a rapid effective forward movement which takes (in frog epithelium) about one-fiftieth of a second, and a slower limp recovery which takes about a tenth of a second. During the former the cilium is rigid and can be prevented from moving by a needle placed in its way, but during the recovery stroke it is flexible and simply passes underneath any obstruction placed in its path. It either changes its state from one phase to the next, or else it is capable of bending in one direction only, that is in the same direction as its effective stroke. A mechanical model of this sort can be made by gluing a row of small wooden cubes on to a piece of linen. If the cubes are in contact with one another bending is impossible away from the linen-backed side, but it is easy in the opposite direction.

Ciliated surfaces nearly always show metachronal rhythm. This means that the cilia of one cell are slightly out of phase with those of the next, which is again out of phase with the next group by the same amount, and so on. The effect of this is that waves appear to pass over the surface. The direction of the rhythm is always the same for one type of tissue, but all three possibilities are realized



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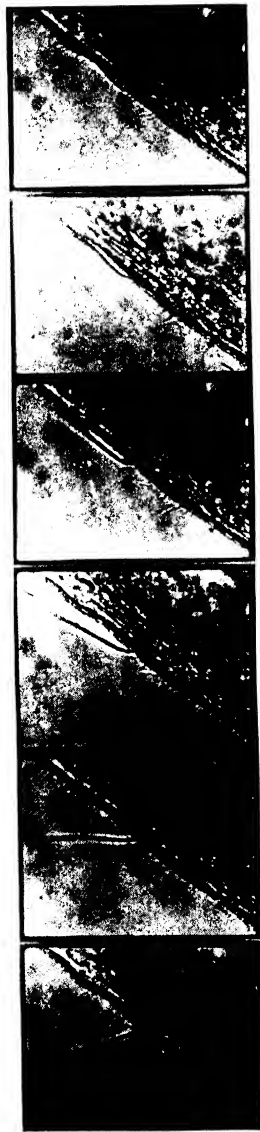
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PLATE II. STILLS FROM A FILM OF CILIARY MOVEMENT

Frames 1-5, recovery stroke; 6-12, effective stroke. (Laterofrontal cilium of *Mytilus*; interval 0.05 sec.). After Gray.

in different forms. In ciliated epithelium from the frog and in the frontal cilia of *Mytilus* the waves travel in the same direction as the effective beat of the cilia, which means that each cilium is a little later than the one just

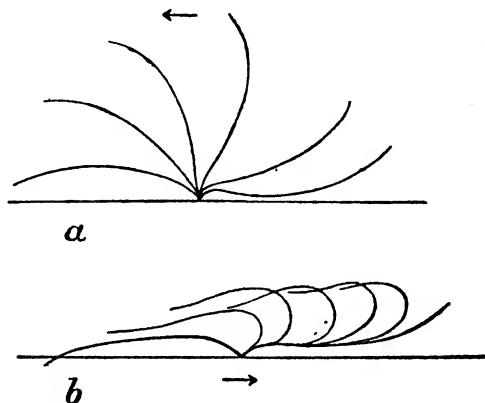


FIG. 21. Diagram illustrating the form of terminal cilia of *Mytilus* during (a) the effective, and (b) recovery, beats. After Gray.

behind it. In ctenophores the metachronal waves travel against the beat. In the lateral cilia of *Mytilus* they go across the direction of beat, so that each cilium is in step with those behind and in front of it, but slightly out of step with its neighbours on each side. The rhythm is upset if a needle is placed in the path of some of the cilia so that their beat is disturbed, but starts again when normal conditions are restored. It is the metachronal rhythm of a line of cilia which produces the appearance of an undulating membrane. In Protozoa an injury to the neuromotor centre upsets the rhythm, and in all cases rhythm stops if the rate of beat is brought below a certain value by narcotics or low temperature.

Flagella, owing to their greater length, are somewhat more complicated, but their movements appear to be

based on successive effective and recovery strokes like those of cilia (Fig. 22). The recovery may start at the base of the flagellum before the effective beat of the tip has finished, with the result that waves travel from base

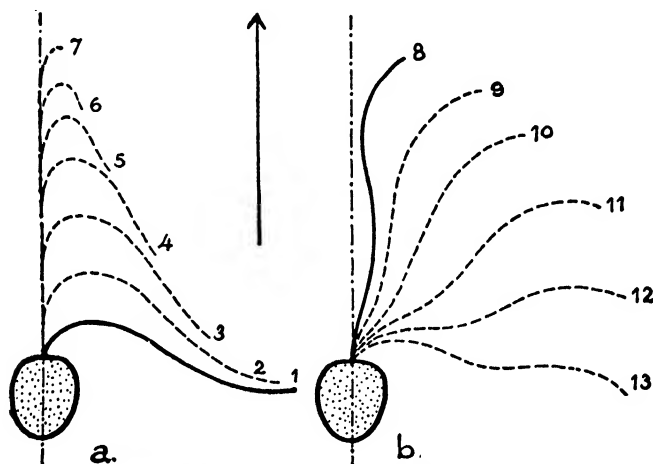


FIG. 22. Simplest type of movement of flagellum of *Monas* during rapid forward movement.

a. 1-7, successive stages in preparatory stroke. Note the flexure begins at the base and spreads to the tip. *b.* 8-13, successive stages in the effective stroke. Note the rigidity of the cilium. The arrow indicates the direction of movement of the organism. After Krijgsman.

to tip. Further, the beat is not confined to one plane. Most locomotory flagella lead the animal, and are called tractella, but a few are posterior and are called pulsella.

There is considerable evidence that both cilia and flagella are not inert things wagged from the base, but are living structures liberating energy along their length. In the first place, the tip may travel through a greater arc than the base, and this is impossible in an inert system. Then there are cases where the tip only of a long flagellum moves, and in most flagellate Protozoa the contraction waves may accelerate.

Cilia and flagella are remarkably free from control by their owner. In the majority of cases they never reverse, and if a piece of epithelium from the roof of the mouth of the frog be cut out, turned through 180° , and regrafted in place, the cilia go on beating in their old way, although they now drive a current down the animal's throat. Reversal does, however, take place in the avoiding reaction of ciliates (see p. 229) and in the food currents of sea-anemones such as *Metridium* (p. 7). The reversal of movement in flagellates like *Euglena* may be brought about by variations in the rate of beat at different parts of the flagellum, without actual reversal. There is only one case on record where cilia can be excited by stimulation of a nerve—in the lip of the mollusc *Physa*—but there are a few cases where nervous stimulation has a depressing influence. If the velar nerve of the veliger larva of the mollusc *Archidoris* is cut or treated with narcotics, the cilia beat continuously instead of intermittently: the nerve must therefore have an inhibitory effect.

Cilia are dependent on the environment in much the same way as other living structures. The rate of beat increases with temperature, but above a certain value changes occur and finally death ensues. With the cilia of *Mytilus* gill, for example, there is a reversible increase of rate up to 28°C ., at 34°C . there is a reduced amplitude, at 38°C . the rate of beat is reduced, at 40°C . the cilia are stationary, at 45°C . they contract, and at 47°C . there is permanent injury and death. In absence of oxygen cilia will go on beating for forty-five minutes, but after this activity slows down, and if they are kept under anaerobic conditions for three or four hours recovery on return to oxygen is imperfect or absent. Cyanides, which upset some of the oxidation systems of the cell (p. 84), have a similar effect. Cilia can therefore put up an oxygen debt (p. 90), but they do not normally do so. This is a suitable

arrangement for structures which work continuously, and is found also in cardiac muscle (p. 91). The respiratory quotient is 0.8, suggesting that energy is obtained by the oxidation of protein. Increase of acidity slows and finally stops cilia, and decreases the oxygen consumption. A balanced solution of cations (calcium and some alkali metals) is necessary, but this may merely be because they are required to maintain the cell-surface. Absence of calcium ion stops the cilia without affecting their oxygen consumption. These facts may be explained by supposing that some reserve of chemical energy, probably a protein, first becomes changed to an active form, and that acidity prevents this process. The active substance breaks down anaerobically with liberation of energy. Absence of calcium ion causes this to be abnormal. Finally, some of the molecules of the break-down products are resynthesized to the reserve by energy supplied by the oxidation of the others. The details of the chemistry are entirely unknown.

4.2. Pseudopodia and Amoeboid Movement

It is difficult to give an exact definition of pseudopodia, but the word is generally taken to mean those projections from a single cell which are of a temporary character and of not very definite shape. Some of the more extreme types exist for quite a long time and have something of the nature of specialized organelles, and all of them are limited in shape by the cell to which they belong. Pseudopodia are found in the Protozoa, in the cells lining the gut in some of the coelenterates, in the wandering cells (phagocytes) of the body fluids of most coelomate animals, and in cells in tissue culture. Those of the Metazoa are all of the same general type, short and blunt, but those of the Protozoa can be classified into four groups. Lobopodia are rounded blunt structures, the typical locomotor organs of *Amoeba*. Filopodia are fine and pointed, and are

found in such amoeboid species as *Euglypha*. Rhizopodia are distinguished by the fact that they anastomose, and are characteristic of the Foraminifera. Axopodia have an axial filament, and are therefore at least semi-permanent in character: probably no satisfactory definition of pseudopodia could be made to include these; they are found in the Heliozoa. There are no sharp dividing lines between the classes; pseudopodia may be made more pointed by increasing the hydrogen-ion concentration or the osmotic pressure of the medium, and blunter by the reverse process. It is at least probable that pseudopodia and flagella are fundamentally the same structures. The axial filaments of axopodia suggest this, and it is supported by the case of *Amoeba flagellipoda*, which possesses a single long thin pseudopodium which moves round in a spiral, like a slowly acting flagellum, once every three seconds. In moribund specimens of the flagellate *Trichomonas* the undulating membrane appears to be replaced by pseudopodium-like projections which move rapidly over the surface. Pseudopodia are often assumed to be primitive, largely because they appear to be unspecialized and because it is traditional to regard *Amoeba* as the lowliest of animals. But pseudopodial formation is certainly not simple, and most protozoologists now regard *Amoeba* as a degenerate probably descended from the Mastigophora, so that flagella are more primitive than, and possibly ancestral to, pseudopodia.

A cell may bear one or many pseudopodia, and they are used for two chief purposes: for ingesting foreign particles and for locomotion. The particles ingested may be food, as in the Rhizopoda, coelenterates, and lamellibranchs; excretory matter in annelids; Bacteria in vertebrates; and tissues of the body which are digested and carried elsewhere during the metamorphosis of Amphibia. The different methods of ingestion of food particles in

Rhizopoda are mentioned in section 1.22. When pseudopodia are used for locomotion it is generally only a single cell which is moved, and in this case the expression 'amoeboid movement' is used to describe what happens; occasionally, however, as in *Hydra* and some other of the Hydrozoa, a larger animal is slowly carried by the pseudopodia of the cells of its base. Amoeboid movement has been studied chiefly in the Protozoa, and has been classified into five groups.

The first is that found in the Mycetozoa, which appear merely to flow over a surface as a liquid film of protoplasm, no well-defined pseudopodia being formed. The second is that exemplified by the normal movement of *Amoeba*, which has been much studied. The chief species which experimenters have used is the marine *Amoeba limax*, which has the great advantage that it forms only one pseudopodium at a time, but other species have been worked with as well. The accounts differ so much that it is possible there is more than one type of movement. To study the movement of the surface of the animal small particles have been dropped on to the upper surface, and then watched. They have been seen to behave in three different ways (Fig. 23): sometimes they maintain their original position relative to the ground, which means that they gradually move to the posterior end of the amoeba; sometimes they maintain their position on the animal, so moving forward at the same speed; and lastly they sometimes move slowly to the front end of the pseudopodium. In this last case they may collect at the front end or they may return along the ventral surface, so that the amoeba has been described as 'rolling like a bag of oats'. The speed of *Amoeba* is of the order of $1\ \mu/\text{sec}$.

The third type is that in which pseudopodia are formed, not in contact with a surface. This happens chiefly when an animal like *Amoeba* is suspended in water. Pseudo-

podia are put out in all directions, and when one of them touches anything solid it attaches itself and the whole mass of protoplasm is drawn into it. Instead of the pseudopodium being withdrawn into the animal, the animal is

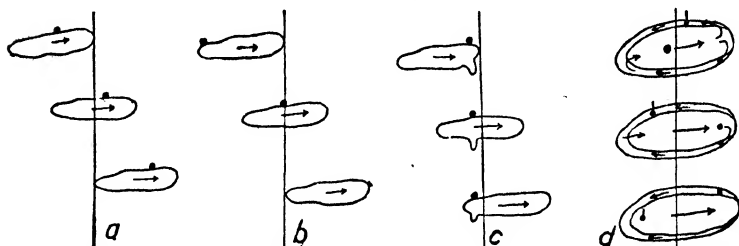


FIG. 23. Motion of *Amoeba* relative to the substratum and to an attached particle.

In *a* the particle is moving at the same speed as the organism; in *b* the particle is moving forward over the surface of the amoeba, e.g. *A. discoides*; in *c* the particle is stationary relative to the substratum, and is moving backwards relative to the surface of the organism; this occurs when attached particles are heavy; *d*, movement of ectoplasm in an amoeba suspended in a jelly. The vertical lines represent a fixed point in the environment. After Schaeffer.

withdrawn into the pseudopodium. Sometimes *Amoeba* moves by a looping movement; one pseudopodium is put out, and after it has stuck to a surface the whole animal moves after it.

The fourth type is found in some species such as *Diffugia* and *Polystomella* in which the pseudopodia become attached by their tips and then contract; when the animal has been drawn up somewhat the same pseudopodia are extended again. This possibly differs in degree rather than in kind from the third type.

The fifth type is the Catherine-wheeling of the Heliozoa. Successive pseudopodia are put out, attached, and contracted, so that the animal rolls on a succession of spokes which it makes for itself. This is the quickest type of amoeboid movement, giving a speed about ten times as fast as that of *Amoeba*.

The effect of temperature on amoeboid movement is

similar to that on all biological reactions. The rate increases up to a maximum, and then falls off rapidly until death occurs. The maximum depends on the normal environment of the animal—it was 40° C. for an amoeba from the Tortugas, but only 20° C. for a very similar species from the English Channel. The maximum is to some extent an artefact, since it becomes lower if the duration of the experiment is increased. Amoeboid movement in the marine *Amoeba limax* is inhibited reversibly at pH 6 and irreversibly at pH 9. As with cilia, a balanced solution of cations is essential. Lack of oxygen does not at first stop movement, but finally it does, and up to a point there is recovery on readmission of oxygen.

These facts point to some chemical basis for amoeboid movement of the same general type as those occurring in cilia and muscles, that is to say of an anaerobic break-down of reserve materials followed by an oxidative recovery. But pseudopodia differ from cilia and muscle-fibres in that they are labile structures, dependent for their very existence on a suitable environment, and much thought has been given to the possible physical processes involved in their formation. One thing that can be said with confidence is that complete satisfaction is given by none of the purely mechanical hypotheses which make pseudopodia the necessary consequences of contact between protoplasm and water of particular viscosity and surface tension. Some chemical reaction is obviously involved, and since oxygen is necessary it is probably of a nature in general similar to other biological processes. The better of the existing theories are all based on the observations that the endoplasm is in active streaming movement, and that at the anterior end of a pseudopodium there is change of endoplasm to ectoplasm. *Amoeba* consists of three layers. On the outside there is a thin plasmalemma, which can be lifted off with needles and is of a dough-like consistency.

Inside this is the plasmagel, which is solid, and includes the classical ectoplasm and some endoplasm; inside this again is liquid plasmasol. The theory of movement is as follows (Fig. 24): at one place the plasmagel becomes weakened

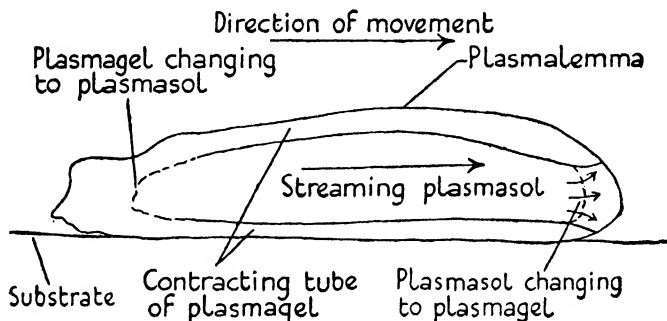


FIG. 24. Locomotion in *Amoeba limax*. Slightly modified from Pantin.

and disappears, and since the rest of the plasmagel is contractile and under tension, plasmasol is forced out at this point. As it comes in contact with the external medium it gelates and so forms a tube of plasmagel. Since plasmagel does not collect at the posterior end, there must there be solution to plasmasol. In addition, for locomotion to take place, there must be attachment to the substrate, and this is the function of the plasmalemma. The movement is rather like what would take place in an imaginary tube of tooth-paste which could squeeze itself out and convert paste to aluminium at the open end and aluminium to paste at the closed end while it did so. This theory does not go greatly beyond observation: gelation at the anterior end can be seen, and sometimes the plasmagel at the end of a pseudopodium is missing, sometimes it is merely thin. If the animal is turgid it is to be expected that slight local alterations in external conditions would be able to produce new pseudopodia by weakening the plasmagel, and this is

found to be the case. The direction of movement can be reversed by pressure and other things (cf. section 6.1). The different directions of movement of a particle dropped on the surface can be explained on the assumption that the plasmalemma has differing relations to the underlying plasmagel. In the typical case it would be expected to be in rigid contact with this, and so particles in contact with it would remain stationary relative to the substrate but move to the posterior end of the animal.

The theory does not pretend to be complete, since fine pseudopodia may be formed from ectoplasm only.

4.3. Muscles

Muscles are made up of individual elongated structures called muscle-fibres, which when stimulated contract in length and increase in girth so that their volume is little altered. So far as the microscope reveals any differentiation at all, it shows that every fibre consists of a number of parallel myofibrils, and that each of these is made up of a chain of contractile sarcomeres embedded in a granular sarcoplasm. The cross-stripping of many muscles corresponds to this arrangement, each sarcomere consisting of a dark band and two half light bands. Each myofibril is continuous throughout the length of the fibre, the apparent divisions being caused by cross-fibres attached to the middle of the light bands. Each fibre is surrounded by a sheath, the sarcolemma. There are many variants on this plan in different groups of the animal kingdom, but since the correlation of structure with function is, except in a general way, obscure, there is no point in going into histological details here. Muscles may be formed from any germ layer, but they are found predominantly in the mesoderm.

4.31. Vertebrate Skeletal Muscle

Vertebrate skeletal muscle is by far the best known of all contractile tissues. It is sometimes called striped muscle,

from its characteristic appearance, and sometimes voluntary muscle, since in man it is, or appears to be, normally under the control of the will. (It is quite obvious that under experimental conditions it is not.) It is innervated directly from the cranial and spinal nerves. Most of the work has been done on the frog, but enough has been done on mammalian tissue to show that it is very similar.

Unlike pseudopodia and cilia, skeletal muscle does not contract unless it receives some definite stimulus, either directly or through its nerve. It may react to pressure, chemicals, or to change of temperature, but by far the most convenient stimulus to use is an electric one: its intensity is easily measured and reproduced and varied, and it is easy to record the exact time of its application. The first things to be said about the working of muscle are therefore concerned with the results of electrical stimulation.

If a small constant current be passed through a muscle there is no visible response, but there may be a sharp twitch when the current is made and another when it is broken. With recording apparatus it can be shown that the make contraction starts from the cathode, and spreads out from there, while the break contraction starts from the anode. It can further be shown that for the break contraction to occur the current must have passed for a certain minimum time. For many purposes it is more convenient to use induction shocks instead of the constant current. It is then found that the current does not pass long enough for the break stimulus to be effective, so that a single induction shock gives a single response, which is a make contraction. It must be remembered, however, that the induction shocks have for physical reasons to be made alternately by opening and closing the primary circuit, and that the secondary current induced on breaking the primary is stronger than that induced on making it. Consequently the contraction of the muscle will be stronger in

the first case. Further, although all the responses of the muscle are make contractions, and start from the cathode,

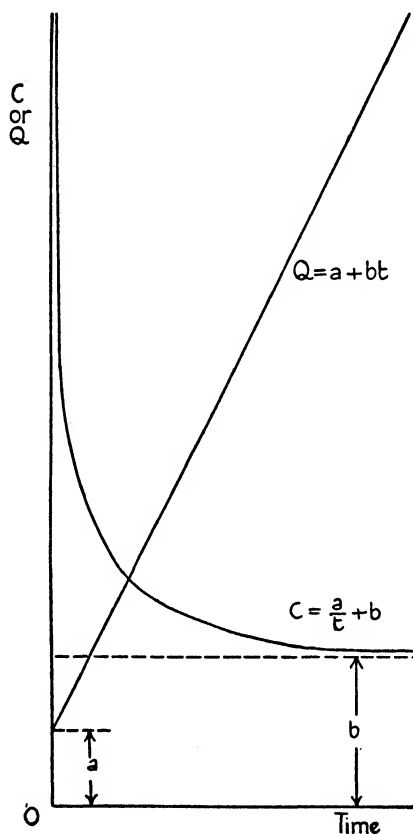


FIG. 25. Curves showing the relationships between current or quantity of electricity in a stimulus and time necessary for response of a muscle. (Weiss's Laws.)

the direction of the secondary current is opposite in the two ways of induction. Single induction shocks are obtained by using a coil with the hammer screwed down.

For obtaining currents of very short duration condenser discharges are used.

It is found that a current of a particular strength must pass for a certain minimum time in order for it to have any effect, and when the current is plotted against this minimum time a rectangular hyperbola is obtained (Fig. 25). The relationship can be expressed by the equation

$$C = \frac{a}{t} + b,$$

where C = the current, t = the time; a and b are constants. b is the smallest current that will produce a response however long it passes, i.e. the value of C when t is infinity. It is called the minimal, liminal, or threshold stimulus, or the rheobase. Since quantity of electricity is the product of current by time, the relation between quantity (Q) and response is easily obtained by multiplying the above equation throughout by t ; $Q = a + bt$, which obviously gives a straight line cutting the y axis at a . This would be the quantity of electricity which passed when an infinitely strong current acted for zero time. It is convenient to express the excitability of a tissue by the chronaxie, which is the shortest time for which a current of twice the rheobasic strength must act in order to produce a response. It bears a simple relation to the constants a and b , for, substituting in the first equation above,

$$2b = (a/t) + b, \quad t = \text{chronaxie} = a/b.$$

The value of the chronaxie for the leg muscles of *Rana temporaria* is 0.7 msec.,¹ but for other muscles it varies widely. In general, the more quickly does a muscle act, the lower is its chronaxie.

If two subminimal stimuli (i.e. stimuli of less than the rheobase) are sent in within a sufficiently short time of one another (about twice the chronaxie) they may together

¹ A millisecond or msec. is 1/1000 second, and is sometimes written σ .

produce a contraction. This is known as summation of stimuli.

When an excised muscle is being used for experimental work it may be so arranged that on stimulation it contracts and lifts a weight, or it may be attached to a spring which is sufficiently strong to move only a little. The first type of response is called isotonic, since it is against a constant resistance, and the second isometric, since during it the muscle does not change appreciably in length. There are certain small differences between the responses under the two conditions, but in general features they are alike. After the application of the stimulus there is a latent period, during which no changes can be observed in the muscle. As usually measured with mechanical levers this is about 10 msec. for the frog gastrocnemius, but if a photographic record of the response is made it can be shown to be very much shorter, certainly of the order of not more than 1 msec. for both frog and mammal, and possibly even less than this. The latent period is followed by the contraction in the isotonic twitch, or the period of development of tension under isometric conditions. The period which this occupies depends on the animal and on the particular muscle used, but in the frog and mammal is generally between 10 and 100 msec.; the isometric response lasts longer than the isotonic. Contraction is followed by relaxation, a passive return to the normal condition. It takes rather longer than the contraction. A tracing for an isotonic twitch is shown in Fig. 26. An increase of temperature reduces the times for all three phases, and slightly increases the rheobase. For normal contraction a balanced solution of ions is necessary.

If a series of stimuli of graded intensity be applied to a muscle, it is found that within certain limits there is also a gradation of response: a stimulus of less than the threshold has no effect, and there is a maximum amount of

contraction or tension which a muscle can show, however big the stimulus which is applied. It is found, however, that so far as individual fibres are concerned there is no gradation: a fibre either responds or it does not, and every

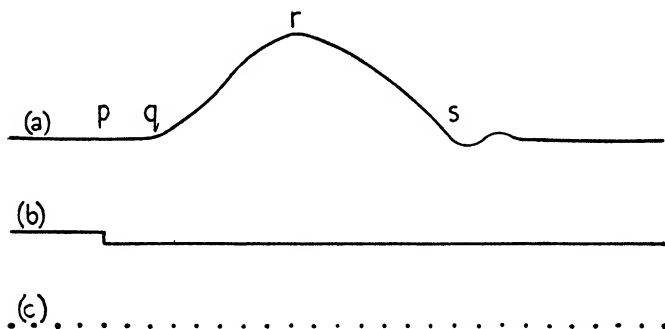


FIG. 26. Tracings of an isotonic contraction of gastrocnemius muscle of toad.

(a) Curve of contraction of muscle; the deflexion below the base line at the end and the subsequent rise are due to the imperfections of the recording apparatus.

(b) Shows point of application of the stimulus.

(c) Shows intervals of 0.02 sec.

pq, latent period; *qr*, contraction; *rs*, relaxation.

response is both maximal and minimal. Muscle is therefore said to react according to the 'all-or-none' rule. Gradation of response in a muscle depends on the fact that stimuli of different intensities cause different numbers of fibres to contract.

The all-or-none rule applies only to varying strength of stimulus under given conditions of experiment, and other conditions may cause differences in the amount of contraction of a single fibre. For example, if the length of a resting fibre is increased by applying a slight tension to it, the response is greater. The contraction or tension of a single fibre can also be increased by applying repeated stimuli. If after the application of one shock a second similar one be given during the rise of the excitatory condition

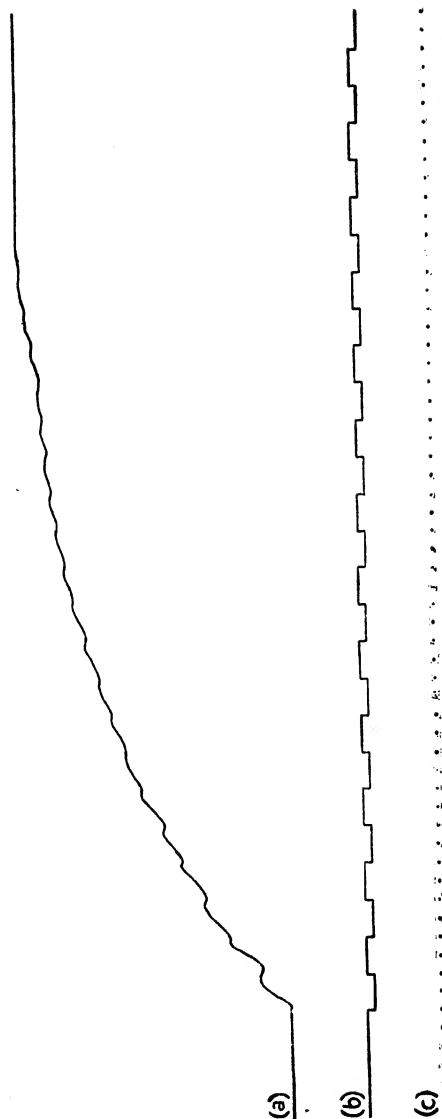


FIG. 27. Tracings showing development of tetanus in isometric contraction of gastrocnemius muscle of toad; five shocks a second: (a) and (b) as in Fig. 26, (c) intervals of 0.1 sec.

due to the first, there is a further contraction, but the magnitude of the response due to the two stimuli is generally less than twice that due to one of them. If a series of repeated stimuli be given, the size of the response is increased to three or four times its simple value, and the contraction or tension is maintained; this condition is known as tetanus (Fig. 27). If the responses do not fuse completely, the resulting incomplete tetanus is called clonus. The maximum interval which can elapse between shocks for there to be tetanus increases with the period of contraction of the muscle. There is also a minimum interval, for if two stimuli are given very close together the response is no greater than it would have been for one of them. There must therefore be a period after the application of a stimulus during which the fibre is not excitable: this is called the refractory period. It is about 5 msec. in the frog, and less in the mammal. It is reduced by raising the temperature. The all-or-none rule follows as a necessity from the existence of a threshold value and a refractory period, for as soon as the first is reached contraction starts, the refractory period sets in, and no further increase in the strength of the stimulus can have any effect. In short, a single muscle-fibre always reacts to a minimal quantity of electricity.

Summation of contractions and tetanus apply to a complete muscle equally with a single fibre, for the muscle is merely a collection of fibres acting individually.

Fatigue is the phenomenon of a muscle refusing to react to a stimulus which normally causes contraction. Complete fatigue is preceded by an increase in the duration of the twitch, and a diminution in the amount of work done. It is due partly to lack of oxygen and partly to accumulation of lactic acid and other products of the chemical process of contraction, and may be abolished by supplying the first or removing the second. It is necessary to

distinguish between fatigue of the muscle and fatigue of the stimulating system. In the ordinary nerve-muscle preparation a muscle which has ceased to respond will still do so if it is stimulated directly, because the junction between nerve and muscle becomes fatigued sooner than the muscle itself. Fatigue, in the ordinary subjective sense of the word, is a mixture of pain due to the accumulation of lactic acid and true fatigue of the motor nerve-cells of the central nervous system. The muscles of a fatigued arm may be made to contract either by direct stimulation or by stimulation of their nerve.

The contraction of human voluntary muscle under ordinary circumstances is of the same general type as that of isolated experimental material. For weak contraction increasing strength is brought about by the use of more fibres, i.e. by quantal summation, but for strong contractions tetanus develops, so that there is fusion of successive contractions of the same fibres, or wave summation. All intact skeletal muscle maintains a certain degree of tension or tonus or tone. This is due to a few fibres contracting for a time, and then relaxing and being replaced by others, so that the tension may be kept up permanently, but none of the fibres ever becomes fatigued. Tonus is caused by nervous stimulation: it is abolished if either the tendon or the motor nerve of the muscle be cut, and is increased by increasing the pull on the tendon. This behaviour is called the stretch reflex, and is very important in some types of locomotion (p. 200). The sense organ concerned in maintaining tone is the muscle-spindle, which is a modified muscle-cell. It is stimulated by being stretched, and through the central nervous system it stimulates a group of muscle-fibres to contract. To give an adequate explanation of tone it may be assumed that this contraction releases the strain on the particular muscle-spindle concerned in the reflex, but increases that on others. The first group

of fibres will, after their twitch is over, relax again, but by this time other groups will have been stimulated to contraction. The muscle as a whole will maintain a certain degree of tension, the exact value of which will be determined by the sensitivity of the muscle-spindles, the period of contraction of the fibres, and other things.

A muscle is a piece of apparatus for doing work, and from the mechanical point of view it may be treated like any other engine. It has been found that in isometric contraction the total heat production (i.e. the sum of energy of all types which is released) is dependent on the tension produced and on the length of the fibres. The exact relation for a single twitch is $H = T.l.A$, where T is the tension, l the length, and A is a numerical constant which varies somewhat, but for which $\frac{1}{8}$ is now considered the best value. The quantity $Tl/8$ is not merely the heat production; it can be shown on theoretical grounds to be the potential energy in a muscle undergoing an isometric contraction, and an important conclusion about the working of the muscle follows from this. By the second law of thermodynamics, heat cannot be converted into any other form of energy without waste, so that the energy liberated by the contraction process (whatever this may be) cannot first be converted into heat and then changed to potential energy, but must go through these forms in the opposite order; in other words, the muscle is not a heat engine.

The stimulated isometric muscle must be in a similar state to a spring under tension: it possesses considerable potential energy, but it can only do work if it is allowed to contract. The ratio which the amount of work which the muscle can do on contraction bears to H is its efficiency. It is found to depend on the rate at which shortening takes place, and this in turn will normally depend on the size of the load. Down to a certain speed, the slower the contraction the larger the work which can be done and

the greater the efficiency, but beyond this optimum value further slowing reduces the work done. The increase of efficiency with fall of speed may be explained on the reasonable assumption that the potential energy which is lost has gone in overcoming resistances to change of shape in the muscle itself (these are generally called viscosity, which in this sense obviously has not its strict physical meaning). It is likely that these resistances would be larger the more rapidly the change was taking place. The existence of an optimum can be understood when it is remembered that work must be done in order to maintain muscle in a contracted state. If the contraction is too slow the work done for this purpose more than counterbalances that saved by reduction in viscosity. For the muscles of the human arm the optimal time for a complete contraction is two seconds, for frog's muscle it is 0.2 sec.

For a tetanic contraction some modification of the equation connecting heat production with tension and length is obviously necessary, and the corrected expression is found to be $H = Tl(A+Bt)$, where t is the duration of stimulation and B is another constant, the value of which depends on the number of twitches which are fusing to form the tetanus. The lower the refractory period and duration of a single twitch, the higher is B . Rise of temperature reduces these and so raises B . A is independent of temperature.

The tension which a muscle develops isometrically depends on its initial length, increasing with this up to a certain value.

More is known of the chemistry of voluntary muscle than of any other tissue, but the matter is complicated and in parts still obscure. The classical lactic acid cycle, with the modifications of it involving phosphagen and adenylypyrophosphate which have been introduced since 1930, are described as an example of energy production on pp. 87-90,

and need not be repeated here. Glycolysis itself is much less important than was formerly thought. The energy for the contraction is supplied by the break-down of either phosphagen or adenylypyrophosphate, and in the absence of oxygen these are restored by lactic acid formation. When, however, the oxygen supply in either frog or mammal is good, lactic acid is not formed, and some unknown oxidative process supplies energy to restore the phosphate esters. In muscles of the cat with blood-supply intact, contraction is followed by an immediate change of muscle oxyhaemoglobin to the reduced form, and some lactic acid formation. When the circulation and respiratory movements have become adjusted to the new needs of the muscle, glycolysis ceases. The apparent importance of lactic acid suggested by the classical work is due to the experiments having been performed on isolated muscles which were always short of oxygen. Carbohydrate is the normal substrate for oxidation, but in starvation muscle is able to obtain its energy from both fat and protein. The manner by which it does this is entirely unknown; there is no evidence to show whether carbohydrate is first formed, or whether the others are oxidized directly.

The chemical processes agree with the heat production. The heat produced by the break-down of adenylypyrophosphate, and that part of the energy liberated by phosphagen break-down which is not immediately used for resynthesis of adenylypyrophosphate, make up the 'initial heat', which is liberated during contraction and at the beginning of relaxation. The glycogen break-down produces the 'delayed anaerobic heat' which is formed during relaxation, and (in the frog) if oxygen is present the oxidation of lactic acid accounts for the 'delayed aerobic heat' or 'recovery heat'. The third of these may go on for a long time after contraction.

When muscle is stimulated not only are there mechanical

chemical and thermal changes, but there is an electrical change as well. If two points *a* and *b* on a muscle are connected to a sensitive galvanometer or an oscillograph, it is found that on stimulation of the muscle a current flows in the circuit first in one direction and then in the other; in other words the instrument records a diphasic wave. The direction of the current is such that *a*, which is the electrode nearer the point of stimulation, first becomes negative to *b*, and then *b* becomes negative to *a*. Since it does not matter where *a* and *b* are, so long as they are on the muscle, this can only be an expression of the fact that a wave of negativity passes down the muscle in the same direction as the wave of contraction. As each point becomes negative to the rest of the muscle a current flows to it in the outer circuit. The electrical change slightly precedes the mechanical change, but the gap between the two is certainly largely, and may be entirely, due to the inertia of the recording instruments for the latter. The better the instruments the smaller it is, and some workers have claimed that it is as little as 0.4 msec. Diphasic waves are a general characteristic of propagated electrical disturbances, and will be further considered in the chapter on nerve.

There are many theories as to the way in which the energy liberated by the break-down of phosphagen or adenylypyrophosphate might be converted to the mechanical energy of contraction. Most of them depend on postulated changes either of osmotic pressure or of surface, but since nothing is known on which a decision can be based it would be fruitless to discuss them here. Whatever the mechanism, it is undoubtedly connected with the peculiar properties of the protein myosin, of which muscle is chiefly composed. One thing is certain, that, as explained above, the chemical energy is not first converted into heat. It is at least possible that the primary change is a physical one, and that the chemical events merely serve to restore energy

used in this. Although much is known about muscular contraction, still more remains to be learnt.

4.32. Vertebrate Plain Muscle

Plain, smooth, unstriated or involuntary muscle occurs chiefly in the internal organs such as the gut, arteries, bladder, and urinary and genital ducts. It has certain histological differences from skeletal muscle, such as the absence of any syncytium, but they are not clearly connected with the physiological differences. The chief of these is that smooth muscle possesses a much greater intrinsic irritability of its own, and with this is correlated its double innervation, one set of nerve-fibres inciting the tissue to contraction, and the other inhibiting it. Between these two types of stimulus smooth muscle carries out the details of its movements automatically, using this word in its strict sense. The motor nerve-fibres which supply smooth muscle are all autonomic (that is their cell bodies are all outside the central nervous system) and they terminate in a plexus in which probably the inhibitory and excitatory fibres are mixed. The two types of fibre have a separate origin as nerves in the central nervous system, the first usually being sympathetic and the second parasympathetic, although the correlation is not absolute.

For experimental purposes nerve-muscle preparations may be made with smooth muscle just as with skeletal muscle. The contraction curves for the two are very similar, but the time relations of smooth muscle are very much slower. The apparent latent period, during which the ordinary arrangement of levers shows no change in the muscle, is from 0.2 sec. to 2 sec., and even the electrical changes do not start till 40 msec. after the stimulation. Contraction itself may last for minutes, and the refractory period is long. Corresponding to this is a high chronaxie, which means that high voltages of short duration, such as

are given by induction shocks, are sometimes insufficient to excite. In these cases the make or break of a constant current must be used. The phenomena of summation of stimuli and summation of contractions are shown. Different effects are naturally produced according to the nerve which is stimulated, but it is not a simple case of excitation from one nerve and inhibition from the other, for the type of stimulus may alter the result obtained. Isolated smooth muscle is very sensitive to other forms of stimulation, such as chemicals, temperature, and mechanical changes. In general it contracts with increased alkalinity, low temperature, and stretching, but effects vary greatly according to the origin of the muscle, its past history, and the mode of application of the stimulus. With some muscles, some kinds of chemical, electrical, and mechanical stimuli, which excite when the tissue is relaxed, cause relaxation when it is already contracted. This is perhaps connected with the double innervation, and may be explained if activity alters the relative excitability of the two types of nerve-endings.

When a stimulus is applied directly to one point of smooth muscle, the contraction may spread over the whole tissue, a result which is very different from the highly individual contractions of fibres of skeletal muscle. Whether the conduction is carried out through the medium of protoplasmic continuity between the fibres, or whether it is merely the nerve plexus that is used, is unknown. Neither is it known whether or not the all-or-none rule applies, but there is no reason to suppose that it does not.

Smooth muscle, whether isolated or in the intact animal, differs from skeletal muscle in that it continually maintains activity of two types. It possesses a certain amount of tonus, and it shows rhythmical contractions superimposed on this: in different places one or the other phenomenon predominates, and occasionally one of them may be absent. They can be explained in terms of the ordinary

muscle twitch by the application of the all-or-none rule. Passive stretch is known to be a stimulus for contraction, and the refractory period is known to be long; tonus will be caused by a synchronous contraction, only a few fibres being active at one time. When these active fibres begin to relax all the other fibres are stretched, but only those which have emerged from their refractory period can respond, and they take over the work of maintaining the tonic contraction. This can go on indefinitely, a few fibres being in activity at any moment, and the rest in a refractory state and waiting to function in their turn. Rhythm may be assumed to be caused by synchronous contraction determined by the nerve net, or by a stimulus carried directly from one muscle-fibre to another where (as in the segmentation movements of the intestine, p. 25) no nervous tissue is present.

The chemistry of smooth muscle is not very well known, but its carbohydrate metabolism is in general similar to that of skeletal muscle, with break-down of glycogen to lactic acid. Phosphagen is present and may be presumed to act as it does in skeletal muscle.

4.33. Vertebrate Cardiac Muscle

As with the other types, cardiac muscle is made up histologically of fibres. Here they are cross-striped, and each consists of several cells placed end to end. Cardiac muscle differs, however, from the other two types in that its fibres are connected to one another by branches; this fact means that the fibre is not the effective unit, and accounts for many of the physiological peculiarities of heart muscle. The all-or-none rule applies to the heart as a whole, so that if any part of the intact organ contracts, the whole does.

For experimental purposes a complete heart, or a strip from some part of the heart such as the ventricle, may be

used. The curve for contraction is similar in general form to that of skeletal muscle, but the reaction is slower. The response of the mammalian ventricle lasts 0.3 sec., that of the frog 0.5 sec. Rise of temperature quickens the response, a correct hydrogen-ion concentration must be maintained, and the heart is very sensitive to the other ions present in the medium. The refractory period is exceptionally long. The absolute refractory period lasts as long as the contraction, and this is followed by a period of subnormal sensitivity while the muscle relaxes. There is a short period of supernormal sensitivity before the normal state is reached. The effect of the long refractory period is that heart muscle cannot be tetanized, which is obviously of great value physiologically. The phenomenon of summation of stimulus is shown, repeated subminimal shocks finally causing a contraction.

The excised heart, whether of the frog or the mammal, will under appropriate conditions go on beating rhythmically for hours, although it is receiving no obvious stimulus. (The correct temperature must be maintained, and in the mammal oxygenated Locke's fluid must be perfused through the coronary blood-vessels which supply the heart.) It seems, then, that there must be some source of stimulation within the heart itself. The situation of this has been investigated by making cuts or ligatures which functionally separate the various parts of the heart. If the sinus of the frog be thus separated from the (auricles plus ventricle), it goes on beating rhythmically, but the auricles and ventricle stop for a time and then start again at less than the normal rate. If a ligature be applied between auricles and ventricle, the first continue beating but the second stops, and either never beats again or does so only very slowly. There is thus a gradient of excitability and of speed of rhythm, which shows that in the normal heart the sinus must act as a pacemaker; the more slowly moving

auricles and ventricle are quite unable to beat in their own rhythm, because they are in physiological continuity with the sinus and so are compelled to beat at the pace of this. The rhythm is entirely independent of nervous origin, for it goes on when the nerves are poisoned by drugs, and it starts in the embryonic chick before any nervous tissue is formed. Isolated cells of heart muscle grown in tissue culture beat rhythmically, so that rhythm seems to be a fundamental feature of cardiac tissue.

The mammalian heart likewise has an automatic rhythm, which is more rapid at the venous end than in the ventricles. In addition to the complete separation of the pulmonary and systemic circulations there are certain anatomical modifications as well (Fig. 28): in particular the muscles of the auricles and ventricles are not in general histological continuity. The pacemaker is the sinu-auricular node, which is a piece of tissue lying between the right superior vena cava and the right auricle, and representing part of the sinus venosus. From this the contraction spreads over the auricles. At the bottom of the auricular septum is another piece of tissue, the auriculo-ventricular node, which also represents part of the sinus venosus. From this starts a band of muscle-fibres known as the bundle of His, or the auriculo-ventricular bundle. It runs in the inter-ventricular septum, and divides into right and left branches for the two papillary muscles. Each branch subdivides so that its fibres are distributed to nearly the whole of the ventricular muscle. It is this bundle which provides the continuity between auricle and ventricle along which the wave of excitation can pass. The rate of conduction is ten times as fast in the bundle as in ordinary muscle, which means that the whole of the ventricle contracts practically simultaneously.

The strength of the beat increases with distension of the heart because as in skeletal muscle the energy of contrac-

tion depends on the length of the fibres. The efficiency is about the same as in voluntary muscle, that is, about 25 per cent.

The chemistry of the contraction of cardiac muscle is

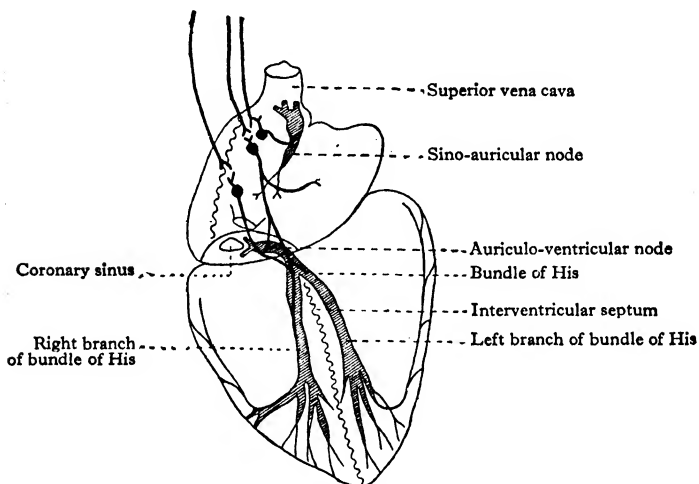


FIG. 23. Diagram to show arrangement of special tissues of heart. After Wiggers.

not known so well as that of skeletal muscle, but there is evidence that in the frog it is somewhat similar. The respiratory quotient of the aerobic heart is 0.85, which suggests that fat or protein or both are used in addition to carbohydrate. The heart will go on beating in nitrogen for hours, although it is then much more sensitive to neutral or acid concentrations of hydrogen ion. Under these conditions the concentration of glycogen is reduced and that of lactic acid increases. In the aerobic heart, on the other hand, glycogen disappears only slowly. It seems therefore that when it is beating anaerobically the frog heart gets its energy as does skeletal muscle by glycolysis, but that under normal conditions there is some other

source as well. This is confirmed by the action of iodoacetic acid, which would undoubtedly stop lactic acid formation. If oxygen is present when this reagent is added the heart goes on beating normally, but in its absence activity only lasts for a short time, about twenty beats. The details of the carbohydrate metabolism of the heart are quite unknown, and they may be different from those in skeletal muscle.

Creatine phosphate and adenylypyrophosphate occur in cardiac muscle, though not in such high concentrations as in skeletal muscle, and it is at least possible that they act in the same way in the two situations. The small amount of phosphagen present would explain the short time for which the anaerobic heart can beat when iodoacetic acid is present.

Events in the mammalian heart may be similar, but judging from the effects of lack of oxygen it is unlikely that it ever beats anaerobically in the living animal.

4.34. Invertebrate Muscle

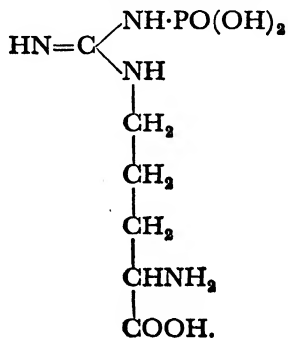
The muscles of invertebrates are much less well known than those of vertebrates, and since the term invertebrate covers several phyla which may be as widely separated from each other as they are from the vertebrates, there is no reason other than that of convenience for grouping them together. Generalization from one phylum is therefore illegitimate, but enough investigation has been carried out to show that in several groups muscular contraction is fundamentally similar to what it is in vertebrates. The contraction curve varies enormously from muscle to muscle; in *Holothuria nigra* the contraction lasts three seconds, but in the wing muscles of the wasp only 5 msec. The rapidly moving muscles, such as those of the limbs of arthropods and the swimming muscles of cephalopods, approximate to vertebrate skeletal muscle, while

the slower ones, such as the intestinal muscle of arthropods and most of those of molluscs, are more like vertebrate smooth muscle. Many invertebrates can maintain many of their muscles in a contracted state for a very long time. Sea-anemones and molluscs of the intertidal zone normally remain contracted for the whole of the time during which they are not covered by water, while the oyster and some other bivalves can remain closed for as long as thirty days. It may be that some special mechanism must be postulated to account for this, but following the Law of Economy of Hypothesis it is better to explain it, as is quite possible, in terms of the ordinary muscle twitch. The muscles of molluscs may be taken as an example. When a lamelli-branch with open valves is touched, the two halves of the shell are drawn together by the adductor muscles, and remain tightly closed until the animal spontaneously opens them again. If a solid object is placed between the valves before stimulation, they shut on this, and if it is gently removed they remain set until they open again or receive another closing stimulus. The tension necessary to open the valves forcibly when they are thus set is much greater than that which will just prevent closure; in other words the adductor muscles can support a weight which they cannot raise. Each adductor muscle contains two bands of fibres of different sorts. These can be separated, and it is found that their properties are very different. In *Pecten*, the one which is striated works at the same speed as frog muscle, and is used for the quick closing of the shell and for flapping the valves in swimming. The other band is much slower in its reaction, having in *Pecten* a relaxation period of about thirty seconds and in the oyster of from a quarter to one hour: it is this which maintains the tension. It may be regarded as acting in the same way as vertebrate smooth muscle which is maintaining tonus, but the tensions reached are very much greater. The state-

ment sometimes made that the mechanism of the maintenance of this tonic contraction must be different from the ordinary process, because there is no increase in metabolism, is hardly correct. On account of the very slow time scale the increase in energy output would be very small, and the classical experiments which are alleged to prove that there are none are not accurate enough to do so.

The same relation between tension and length has been shown to hold for muscles in *Mytilus* and *Helix* as for frog muscle. Of the chemistry of invertebrate muscle little is known. Phosphocreatine is found only in *Branchiostoma*, the Enteropneusta, Pleurobrachia, and the Echinoidea and Ophiuroidea. The first two of these are primitive chordates, and although necessarily classed as Invertebrata are more nearly related to the vertebrates than to any other phylum of invertebrates. The last two belong to the Echinodermata, the phylum which on embryological grounds is considered to be most nearly related to the chordates. (It is perhaps suggestive for the classification of the protochordates that in the third sub-phylum of them, the Tunicata, no creatine phosphate has been found.)

In invertebrates the place of creatine phosphoric acid seems to be taken by arginine phosphoric acid, a somewhat similar compound with the formula



Like phosphocreatine, this can break down, liberating energy and phosphoric acid, and so is called a phosphagen. It has been found in platyhelminths, annelids, arthropods, molluscs, and echinoderms, as well as in tunicates and enteropneusts. It is probable that there are other phosphagens as well, and this may account for the fact that the calculations which have been made to try to relate the resynthesis of arginine phosphoric acid with lactic acid formation do not work out as nicely as those for vertebrates. There is, however, little doubt that the energy for muscular contraction in invertebrates is obtained by some sort of phosphagen break-down, followed, under anaerobic conditions, by lactic acid metabolism. It is unlikely that the details of the latter are the same as in vertebrates.

4.4. Glands

Glands are organs which secrete, and secretion means the preparation of a material and its extrusion from the cell. As to the properties and purposes of such materials, each gland must be considered separately, and an account of the functions of a good many of them is found here and there in this book, particularly in sections I and V. Yet there remains something common to all of them which must be considered here, for glands are very important effectors.

The formation of material goes on inside cells, and all observations on the early stages of secretion are essentially cytological ones. The first phase is the reception of material, and of this little can be said; it is similar to other cases of passage through a living membrane, and at least at times requires energy. Next comes the actual chemical process of formation of the material. It is assumed that this is aided by enzymes, and there is much circumstantial evidence that both the mitochondria and Golgi bodies are used in the process. The Golgi apparatus

increases in size during secretion in glands of many different types, as well as in the cells of the intestinal epithelium during the resynthesis of fats. In the cells of the pancreas the secretion appears as granules, so that its formation can be watched. If the mitochondria are destroyed by X-rays, as they can be without any other apparent damage being done to the cell, no more secretion is formed until they reappear, which is not until a few hours after radiation. The nucleus also seems to be necessary for metabolic processes such as secretion, for while separated parts of Protozoa without nuclei can move and ingest food, some authors have stated that they cannot digest; enucleated plant protoplasm cannot form cellulose, nor can adult mammalian erythrocytes make haemoglobin. The nucleus in gland cells is often found to be near the part of the cytoplasm which is most active, and sometimes it shrinks and shrivels during secretion, which suggests that substances pass out from it. The method by which the nucleus and the cytoplasmic inclusions act is unknown, but it has been suggested that the function of the mitochondria is to provide a surface at which reactions can take place.

In vertebrate salivary glands and some others it has been shown that there is an increased oxygen consumption and a rise of temperature during activity.

Extrusion, which may be brought about by a stimulus given by nerve or hormone, is accompanied not only by rise of oxygen consumption and heat production, but by electrical changes as well. It takes a number of different forms. The granules of secretion may be dissolved and go out in bursting vacuoles, as in the pancreas, or as much as half the cytoplasm may be lost with the granules. This happens in the mucus-secreting cells of the intestine of Amphibia, in the midgut and salivary gland of the snail, and in sweat and lacrimal glands. The nucleus and

sometimes parts of the Golgi apparatus and mitochondria remain. In some extreme cases, as in the midgut of the crayfish and in sebaceous glands, whole cells may be lost, so that each cell secretes but once, and the gland is only maintained by rapid mitosis. Secretion is a cyclical process which goes on without any apparent outside stimulus, but when the cells are exhausted by repeated stimulation the formation of material takes place more rapidly than usual.

4.5. Electric Organs

Electric organs are sufficiently described by their name. They are found only in fishes, and are particularly well developed in the three species *Gymnotus electricus* (the electric eel), *Malopterurus electricus* (the electric catfish), and *Torpedo marmorata* (the torpedo or electric ray). While small electric changes are accompaniments of almost all biological reactions, it is only in electric organs that the production of a relatively big potential difference is an important function.

In all cases the organ is made up of a number of disks or compartments, which in *Malopterurus* are modified skin glands, but which in all the other species are derived from striped muscle. They are so arranged that the voltages due to the separate disks are summed; in short, the disks are in series. The voltage for each compartment varies, but is about 0.04, which gives a total potential difference for the whole organ of 200 volts in *Malopterurus*, 300 in *Gymnotus*, and 30 in *Torpedo*. The motor nerve to the organ has a number of branches which supply each disk individually. The arborization of the nerve occurs always on one side only of the disk, and the current in the organ flows from this side to the other. The nervous side is therefore the negative pole. (The direction of the current in *Malopterurus* is exceptional.)

Nerve-organ preparations, similar to the common nerve-muscle preparations, have been used for experimental study, and the results obtained are in a general way similar to those for muscle. An electric organ responds with difficulty to chemical reagents, but easily to mechanical shock. For electrical stimulation the rheobasic current is about one hundred times that for the frog's gastrocnemius. There is a latent period of about 10 msec. at 5° C. and 3 msec. at 30° C. The preparation can be fatigued, but is relatively indifferent to drugs such as curari and atropine. There is no spread of excitation from one disk to the next other than by nerves, but each discharge is rhythmical, because the current produced by the first discharge excites the nerve and so stimulates a second discharge, and so on. There is thus, for one primary stimulation, a series of successive discharges at a frequency which varies with the temperature but is of the order of 100/sec. There is, however, a decrement in successive discharges, and the whole series seldom lasts more than half a second.

The ordinary reflex discharge in the intact fish is also a rhythmical one, but the rhythm here is due to the stimulus from the central nervous system, for its frequency depends not on the temperature of the organ, but on that of the ganglion from which the nerve starts. The reflex discharge is given on the receipt of various sensory stimuli by the fish, particularly by mechanical pressure on the skin. *Gymnotus* is stimulated to discharge when live fish are placed in the same tank; some of them are stunned, and the eel, which swims only slowly, is able to catch and eat them. Electric fish are themselves relatively insensitive to electric shocks, so that they are not affected either by the voltage from their own organs, or from other fish in their vicinity.

Of the details of the physiology of the organs little is

known. The time relations are by no means clear, for while it is obvious that if the voltages of the separate plates of tissue are to be summed, as in fact they are, discharge in all of them must be simultaneous, it is impossible to see how the time of receipt of the stimulus can be the same for all of them, when the organ may be as much as 30 cm. long and the nerve enters at one end. There is some evidence that the organ acts as a concentration cell, which agrees with its high efficiency: an average value in *Torpedo* is 60 per cent. It was shown in 1937 that phosphagen occurs in the electric organs of *Gymnotus*, and that the general biochemical relations are similar to those of muscle. This agrees with the morphological opinion that the electric organ is modified muscular tissue.

4.6. Luminescent Organs

It is possible that a good many of the chemical processes which help to make up the phenomena of life are accompanied by a fortuitous emission of electromagnetic radiation. A number of Russian workers have claimed to have detected rays of wave-length about 2,000 Ångströms which are given off when cells divide. Such radiation, called mitogenetic, could not be detected in Great Britain in a careful search for it by using a Geiger counter, and so many biologists consider that it has no real existence. The Russian evidence for its existence is consistent and increasing, but its intensity must certainly be very small. An observer has also reported that living mice emit infra-red rays, by means of which owls are able to find them in the dark. The eye of a young tawny owl (*Strix aluco*) was found to be sensitive to rays as long as 15,000 Ångströms, and although it could find living mice in the dark it was unable to find dead ones unless they were illuminated with infra-red light.

Apart from these rather doubtful cases there are many

in which no apparatus is necessary to detect the radiation given off, because it lies within the range of wave-lengths to which the human retina is sensitive. Such animal light is produced by representatives of about forty orders of animals, distributed through nearly all the phyla. It is found in the Protozoa (Radiolaria and Dinoflagellata); in all three classes of Coelenterata and in the Ctenophora; in Polychaeta and Oligochaeta; in the Ophiuroidea; in four classes of Crustacea, in the Chilopoda, and in many orders of Insecta; in the three main classes of Mollusca; in the Hemichordata and Urochordata, and in both Elasmobranchii and Teleostei. It is noticeable that all the forms which possess it are either marine or terrestrial, but the significance of this is unknown. The fish alone, and not all of them, luminesce continuously, all the others needing some stimulus to start them. In this the animals differ from the light-producing plants—Bacteria and Fungi—which are permanently luminous. The uses of the light vary with the species emitting it. In the planktonic forms such as the dinoflagellate *Noctiluca* no function can be assigned to it, and it is probably merely a useless but necessary accompaniment of a chemical reaction which goes on for other purposes. This sort of light would then be ecologically similar to the rather vague non-visible radiations mentioned at the beginning of the section. In many others, such as the fireflies (Coleoptera of the genera *Photinus* and *Photurus*) and the glow-worm (a beetle called *Lampyrus*), and some worms and fishes, the light is produced chiefly or only in the breeding season. From this fact, and from the behaviour of the animals, it seems clear that the light is used as a sex signal, and is thus of the same sort of use as the bright colours of birds or the scent produced by many female moths. Luminous animals living in the deep sea (fish, squids, and shrimps) often have complex organs with reflectors and lenses which throw the light in

a beam. Here it seems likely that the animal is providing its own artificial light in a region where there is no daylight.

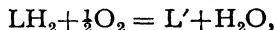
All animal light disappears irreversibly when the tissues are boiled, so that it seems that an enzyme reaction is involved, and it has been shown in many cases, following the original observations of Robert Boyle, that oxygen is necessary. As a general scheme for all animals it may be said that light is produced by an enzyme oxidation. The substrate is called luciferin and the enzyme luciferase. Since these are not the same in all animals the words should be regarded as generic names and may be used in the plural. The luciferin is almost universally manufactured by living cells in the form of granules which may either be oxidized within the cell as in insects and most fishes, or may be extruded as a secretion, as in most Crustacea and annelids. More is known of the latter type, particularly in the ostracod *Cypridina*. In this the granules dissolve in the sea-water and the light is emitted from the resulting colloidal solution. In others, such as the fish *Malacocephalus*, the granules do not dissolve, so that under the microscope discrete points of light can be seen.

Luciferin and luciferase have not been demonstrated in all the groups of luminous animals, but they have been found in the worm *Odontosyllis*, in *Cypridina*, in fireflies and beetles, in the lamellibranch *Pholas dactylis*, and in *Malacocephalus*. The luciferases are non-specific, but only within a fairly narrow range; those of the fireflies and other beetles are active with the luciferins of each other, but not with that of *Cypridina*, which is a member of the same phylum. *Cypridina* luciferase is non-dialysable, is destroyed by trypsin, and is insoluble in fat solvents but soluble in water, from which it is precipitated by saturated ammonium sulphate but not sodium chloride. In other words it has the proper-

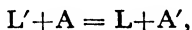
ties of an albumen. Luciferin from the same animal is dialysable, is not destroyed by trypsin, is insoluble in ordinary fat solvents, but is soluble in alcohol as well as water. Its nature is unknown, but it does not appear to be a protein. In alkaline solution in the air it readily oxidizes spontaneously, but in the absence of oxygen it has been kept stable for ten years.

The production of the light is concerned rather with the luciferase than with the luciferin, for when the latter is oxidized in other ways no light is emitted. Furthermore, when luciferase and luciferin from different species are mixed, the spectrum of the light is that characteristic of the animal supplying the enzyme. Free oxygen is also necessary, for when luciferin is oxidized by luciferase in presence of potassium ferricyanide but in absence of oxygen, no light is produced.

On these and other facts the following theory of the reaction is based: luciferin (LH_2) is oxidized by molecular oxygen to oxyluciferin (L) with luciferase as a catalyst. After this reaction the luciferin is left with excess of energy, or in an excited state, so that the equation may be written



where L' represents an excited molecule of oxyluciferin. The excess of energy and excited state is then transferred to the luciferase (A),



and this then returns to its normal state, giving out its excess energy in the form of radiation,



Such a reaction is known as a sensitized photochemical reaction. The spectrum of *Cypridina* has a maximum at $\lambda = 4,800$ Ångstroms and is a broad band, which fits the theory of this type of reaction. Quantitative studies on the

reaction show that of the order of one hundred molecules of oxygen must react to give one quantum, which means that only one collision in a hundred is effective in producing the necessary active state.

4.7. Nematocysts

The nematocysts of coelenterates are peculiar effectors which are produced in special cells called cnidoblasts, but which are not themselves living. When fully formed, a nematocyst consists of an ovoid sac or capsule which has a tough wall which at one pole is invaginated to form a tube; the latter has a wide basal portion, and then a longer coiled narrow part. The inside of both parts of the tube usually bears spines, arranged in whorls of three at different levels. The base of the tube, where it is continuous with the walls of the capsule, is closed off from the outside by an operculum. The capsule is filled with liquid. After the nematocyst has been discharged its structure is not essentially altered, but the operculum has burst and the tube has been evaginated, so that it projects into the surrounding medium and its spines are now on the outside. In an average nematocyst the tube is $700\ \mu$ long, but there is much variation. Seventeen different varieties based on this general plan have been recognized, and of these four are present in *Hydra*. In the first type, which is large, the tube has a well-defined basal portion which is dilated at its base; spines are restricted to the upper part of the wide tube, and the three lower ones are much longer than the others; the tube is open at its end. Two of the other types are small and have a tube which is isodiametric along its whole length and open at the end, and differ only in that the one bears spines uniformly to its end while the other has none. The fourth type has much reduced spines, and the tube evaginates in the form of a corkscrew and is closed at the end.

The cnidocil is a short projection at the side of or on top of the operculum, but it is often absent. The base of the cnidoblast is elongated and rests on the mesogloea, but there is no evidence that it is attached to a nerve-cell. The cnidoblast may start in either ectoderm or endoderm or as an interstitial cell, according to the species, and undergoes a complicated migration before it comes to rest in its definitive position. In some cases it even passes through the enteron, being carried by the flagella of the cells lining that cavity. The chemical nature of the capsule and its contents is quite unknown, but the wall is certainly not made of chitin.

The process of discharge is always an evagination, and takes from one to three seconds. It can be slowed down and observed under the action of chemicals, and a cinematographic record of it has been made. The appearance of the wall of the capsule does not change and its volume, although it usually alters slightly, does not change in any regular way. The tube, on the other hand, increases in size, sometimes to double its resting diameter and length. The spines may remain attached or they may fall off, and several may stick together as they fall, forming a sort of harpoon. In some cases the contents of the capsule can be stained with neutral red, and the discharge, which is then slowed down, can be watched under the microscope. No liquid comes out of the tube until evagination is complete, but before this the contents, both of capsule and tube, break up into coloured and colourless drops. Liquid then comes slowly out of the end of the tube; the colourless parts immediately disappear in the water, but the coloured drops run together and dissolve only slowly. The volume of liquid which goes out is greater than that of the original capsule, and some coloured liquid remains inside. In those nematocysts which have a blind tube no liquid leaves it, but the capsule swells on discharge.

Several theories have been put forward to explain the discharge, but the only one which agrees with observation is that which states that it is due to osmotic swelling.

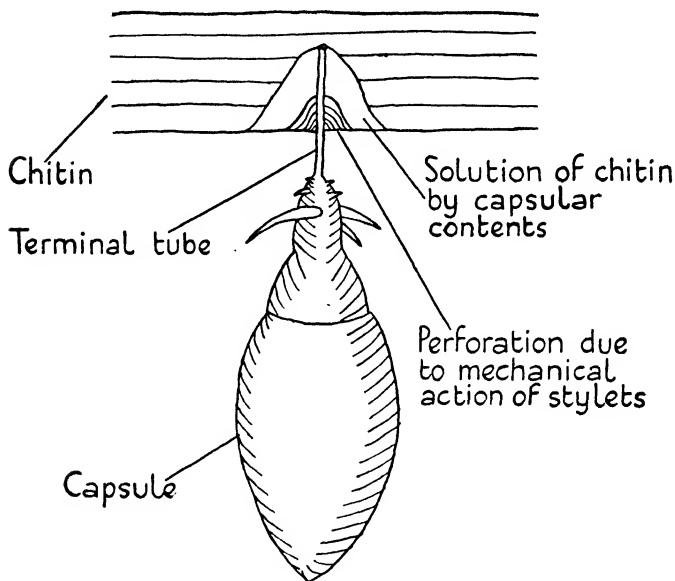


FIG. 29. Nematocyst of *Hydra* with the tube perforating the chitin of an arthropod. After Toppe.

Some stimulus (experimentally a hypotonic solution or a strong reagent such as an acid or base) bursts the operculum, so that the outside medium comes in contact with the wall of the invaginated tube. This is semipermeable, and the capsular contents have a high osmotic pressure, so that water is absorbed. The increased internal pressure evaginates the tube, and forces out some of the contents. Since there is no connexion with nerve-cells, and since isolated nematocysts discharge perfectly well, there is no evidence for nervous control. It has been suggested that the cnidocil is a chemoreceptor, reacting to chemicals in

the medium, but as it is often absent it cannot be a necessary structure. There is no evidence that contractile fibres help in the discharge except that in some cases they may assist in breaking the operculum. The normal stimulus for discharge, except that it is the presence of foreign bodies, remains unknown.

The precise function of the nematocyst also remains uncertain. Cnidaria are surely on the whole able to sting, but the stinging properties of jellyfish as judged subjectively by man seem to be quite independent of the discharge of nematocysts, and it is at least possible that the poison is not produced by these effectors at all. Some animals are quite immune to the attacks of coelenterates and even feed on them, but it is not known whether this is true chemical immunity or whether these animals just do not stimulate the cells to discharge. In a few cases, notably for the large nematocysts of *Hydra*, it has been shown that the spines pierce chitin mechanically, and that the tube enters the perforation which is enlarged by solution (Fig. 29). The smaller types possibly assist in holding the prey or in attaching the hydra to its base, but their value is rather doubtful. Some types of nematocyst, with a closed tube and no spines, have been said to have no conceivable function whatever.

4.8. Chromatophores

It is convenient to include under the name of chromatophore all cells near the surface of an animal by which it can make temporary changes in the colour or shade of its skin. Such cells are found in molluscs, Crustacea, and all three classes of cold-blooded vertebrates. The word is not applied where a colour change is caused, as in blushing, by changes in blood-content of the superficial vessels, nor where a prolonged change such as the tanning of the skin on exposure to the sun is brought about by the development of fresh pigment. A chromatophore is a cell

which contains a quantity of pigment which varies in its disposition. Where the pigment is black the name melanophore is often used, and corresponding words derived from the Greek have been used for other colours.

A chromatophore of a cephalopod consists of a pigmented cell to the outside of which are attached several radiating muscle fibres which are in the plane of the surface of the body. When these contract, the cell is drawn out to its maximum size, and if all the chromatophores in one part of the skin are in the same state the area will have the colour of the pigment. When the muscles relax, the cell by its own elasticity contracts to a point, and the pigment therefore contributes little to the colour of the skin as a whole. Differently coloured cells may be present, and by the independent action of these very varied colours are produced. The system is one of muscle controlled by nerves and hormones, and calls for no special comment.

The typical chromatophore is found in the Crustacea (almost exclusively the Malacostraca insects) and vertebrates. In all of these it is a cell (or sometimes a syncytium) with branched processes, and it is the movement of the pigment into and out of these which causes the colour change (Fig. 30). As in the molluscs, expansion of the pigment produces colour or a dark condition of the skin, and its contraction produces pallor. Chromatophores of different animals differ widely in the way in which they react to stimuli, and above all in the way in which they are controlled. In most cases they need a stimulus for both expansion and contraction, so that it is impossible to say what is their resting and what their active state. Only when the particles are moving do they show Brownian movement, so that perhaps this condition is the active one, and any state where the particles are stationary a passive one. There is no reason for regarding chromatophores of this type as being modified smooth muscle.

In the shrimp *Crangon* there are four different pigments, brown, white, yellow, and red, which are distributed amongst the chromatophores in all possible ways except that brown is always present. By appropriate movements of the pigment the animal matches itself to any back-

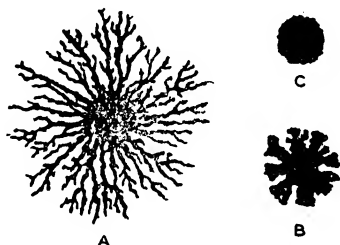


FIG. 30. Melanophores of *Fundulus* in three stages.

A, fully expanded; B, stellate; C, fully contracted, punctate.
After Parker.

ground which comes towards the red end of the spectrum. Other Crustacea are similar, but not so complicated. If both eyes of the animal are excised there is no response to a changed background, the chromatophores remaining permanently expanded, so that the eye is clearly the organ which receives the stimulus. The means by which the pigment was made to move was for long undecided, but it was shown in 1928 that the eye-stalks secrete a hormone which travels in the blood and causes the contraction of the pigment. In *Crangon* and some other genera another hormone has been found, which is formed in the rostral region and which causes expansion. The first has been called contractin and the second expantin; they are not specific. The control of crustacean chromatophores is therefore clearly humoral, but it is obvious that the complex colour changes of *Crangon* are by no means fully explained. Recently it has been reported that in blind specimens of *Hyppolyte varians* the chromatophores can contract under the direct action of light as well as when

stimulated by hormones. The isopod *Ligia* is similar to the decapods.

Many fish possess chromatophores, and their colour changes range from a mere passage from white through grey to black, to an ability to take up almost any colour of the spectrum. In some cases chromatophores with different pigments have been found, and it is likely that such occur wherever there is a real change of colour as opposed to a mere change of intensity. In the teleosts, as in the Crustacea, excising the eyes or covering them inhibits the response. It is interesting that when the fish is on a dark background it is dark, but when it is in complete darkness it is pale, so that being in the dark and seeing black are not the same thing. The chromatophores have been shown by histological preparations to have a good nerve-supply, and if the nerves to an area are cut in such a way as not to hinder the blood-supply, the skin of this part maintains a uniform grey colour, while the rest of the body may change and become lighter or darker according to the background. Both expansion and contraction are, then, under nervous control. In *Fundulus*, which has yellow xanthophores as well as melanophores, the two types of cell are under independent control, so that on a yellow background the xanthophores are expanded and the melanophores contracted. It seems likely that a similar explanation would account for the more complicated colour changes of other fish, but this has not actually been shown to be the case. Some fish assimilate their body to a mottled background with considerable success, and even make a fair attempt to copy an artificial chessboard pattern on which they may be placed. The response is here a complex one involving independent behaviour of chromatophores in different parts of the skin. There is some evidence that in *Fundulus* there is double innervation of the cells, and dispersion may perhaps be

parasympathetic and contraction sympathetic. The nerves undoubtedly act on the chromatophores by secreting a substance which acts directly on them (see section 5.32).

In some bony fish, and in all the elasmobranchs which have been studied, hormones are used as well, apparently the same B and *w* substances as are found in Amphibia (see below). In the eel *Anguilla vulgaris* and the stickleback *Gasterosteus aculeatus* the humoral control works alongside that by nerves. In the dogfish *Mustelus canis* pallor alone is caused by stimulation of nerve fibres, darkening by a hormone. The catfish *Ameiurus* behaves like *Fundulus*, but at the same time dispersion is normally produced by the action of the pituitary. Three species* of *Raja* and two of *Scyllium*, including the common roughhound, go even farther than *Mustelus*, for their chromatophores have no nervous control, but are regulated entirely by hormones.

Many of the Amphibia change the colour of their skin, just as do fishes, so that it resembles the background, but at the same time they react to other stimuli as well (Pl. I). In general, pallor is produced by a light background, dryness, or a relatively high temperature, and darkening by a dark background, moisture, and a low temperature. Being in the dark has the same effect as being on a dark background. Where two of these stimuli are in opposition to one another, one may be preponderant or a balance may be struck; so that the eight possible combinations give, in the common toad, the following order of decreasing blackness:

- Cold wet on black background
- Cold dry on black background
- { Cold wet on white background
- { Hot wet on black background
- Hot dry on black background
- Cold dry on white background
- { Hot wet on white background
- { Hot dry on white background.

Cold means on ice; hot, at about 20° C.: wet is in a closed vessel containing water; dry, in a closed vessel containing calcium chloride. The actual chromatophores are similar to those of the fishes, and the changes in colour are produced by actual migration of pigment; cells of two different colours may be present. A further point of similarity is that response to light is nearly, but not quite, abolished when the animal is blinded. It must therefore be admitted that although the eyes are the chief sense organs involved, yet the Amphibia also possess photo-receptors in their skin.

Here, however, the similarity ends. No nerve-supply to amphibian chromatophores has ever been demonstrated, and experiments on nerve-cutting have shown that nervous control has scarcely any effect on them; it certainly has no part in the ordinary colour responses of the animal. On the other hand it has been conclusively shown that control is by the pituitary gland; if this gland, or its posterior part, is extirpated the frog becomes uniformly pale under whatever conditions it may be placed; and if extract of pituitary be injected into such an animal the chromatophores gradually expand. The expansion is, however, only temporary, so that either contraction is the resting state of the cells, or more probably another hormone is at work. Further more detailed investigation has shown that at least three influences co-operate in determining the colour of Amphibia. There is first a primary response in which the chromatophores react directly to light by expansion. This is generally subordinate to the other two influences, but in a few genera such as *Necturus* it is predominant. The secondary response is the co-ordinated one which, as seen in the common frog, generally assimilates the animal to its background and which is worked through the eyes. It is carried out by two pituitary hormones; the B substance, produced by the

pars intermedia, causes darkening, and the *w* substance, probably formed in the pars tuberalis, causes pallor. Adrenalin also can cause pallor, but whether it ever acts in the natural state is unknown. The hormonal control, which is necessarily generalized, adequately explains why the colour change is slower than in fish, and why the Amphibia cannot imitate a chessboard pattern.

But few reptiles can change their colour, and those which can belong mainly to the Lacertilia. The chameleon is proverbial for the many colours which it can take up, but it does not ordinarily resemble its background. Reptilian chromatophores are in general similar to those of other vertebrates, but in addition they act in part by covering or uncovering stationary masses of pigment in underlying tissue. The physiology of the response has been worked out in only a few cases, but in general, bright illumination and low temperature produce pallor, while darkness and high temperature cause the melanophores to expand. In addition, any noxious stimulus produces pallor, and the animal is lighter on a white background than on a dark one. As before, the eye is the receptor for the response to light, but there is direct action on the skin as well. In the chameleon the melanophores are under direct nervous control; electrical stimulation of the roof of the mouth induces pallor only in those parts of the skin to which the nerve-supply is intact. In *Phrynosoma* (mis-called the horned toad) there is double control, pallor being produced either through the nervous system or by the liberation of adrenalin into the blood-stream. A scheme which works for the chameleon is as follows. An autonomic discharge *E* keeps the melanophores in a state of contraction comparable to tonus in muscles. This may be inhibited by afferent impulses *a* caused by light falling on the skin, and by other afferent impulses *b* which come from the retina when the animal is on a dark background.

Afferent impulses w which the retina sends in when the animal is on a white background suppress a . The total responses of the animal are therefore as shown in Table 4.

TABLE 4
Responses of Chameleon. (From Sand)

<i>Environment</i>	<i>Nervous impulses</i>	<i>Condition of chromatophores</i>
Darkness	E	Contraction
Blind animal in light	E, a	Expansion
Normal animal on black background	E, a, b	"
" " white "	E, a, w	Contraction

This scheme works also for the minnow, *Phoxinus*, except that incident light acts not directly on the skin but on a parietal organ, but it is not fully successful with other fishes and reptiles.

No other effector shows such a varied and complicated type of control as does the chromatophore. Sometimes it is humoral, sometimes nervous, and it is noteworthy that in the vertebrates nervous control seems to have been given up in the Amphibia and regained in the reptiles. (It must be remembered that none of the existing orders of Amphibia is anywhere near the presumed ancestry of the reptiles.) Where the control is humoral there is little specificity, extract of the partes nervosa and intermedia of mammals being potent in causing expansion in Amphibia, and mammalian adrenalin causing contraction in both reptiles and amphibians. It has even been shown that extract of the eye-stalks of prawns will induce contraction of the melanophores of plaice.

V

CO-ORDINATION OF FUNCTION

IT has been pointed out on p. 117 that most effectors need to be stimulated into activity by some influence which they receive from elsewhere. If this were not the case, if effectors were all independent, no co-ordination would be possible: each small part of the body would act solely in accordance with the stimuli which it itself received. The mechanism which conveys the stimulus from the receptor which picks it up to the effector which reacts to it, and so ensures concerted action by different regions of the body, is called a co-ordinating system. There are three types of this, but it is possible that all three are really developments of the same fundamental method.

5.1. Hormones

It is convenient to begin with the method which was the last to be discovered, that in which a gland discharges into the blood-stream a chemical substance which acts on a distant effector. Co-ordination of this sort can obviously only occur in animals with a vascular system; the first case to be worked out, that of the stimulation of the pancreas, was published by Bayliss and Starling in 1902. The substance passed into the blood-stream is called an internal secretion or autacoid, or, most generally, a hormone. The gland which produces it is called a gland of internal secretion, or an endocrine or ductless gland. In a general way an organ may be predicted to be an endocrine gland if it has obviously secretory cells but no duct; this was the case with the islet tissue in the pancreas, which was forecast as an endocrine organ ten years before its hormone, insulin, was discovered or its function known. The grounds for such a prediction are strengthened when pathological

changes in the gland are associated with clinical signs of disease. The normal way of testing for endocrine action is, first, to remove the suspected organ from an animal and observe the effects. Extracts of the organ are then injected into the blood; if this restores the animal to normal, endocrine action may be taken as proved. In some cases the active part of the extract is now well known, and can be shown to be liberated into the blood in the normal state. Little of a general nature can be said about hormones. A gland, stimulated in most cases by a message sent from a sense organ through the nervous system, produces a chemical substance which is carried in the blood to an effector which it causes to react. The method by which the last link happens is in no case known. The degree of specificity of hormones varies, but in general they act on a particular type of tissue rather than on a particular organ. It is possible to make two generalizations about the properties which hormones must possess if they are to be effective; they must be able to escape from the blood-vessels fairly easily, and they must be destroyed fairly readily in the body. If the first condition were not fulfilled response would be very slow, and if the hormone remained in the body indefinitely its effects would likewise be permanent. Such of the hormones as have been isolated have a comparatively low molecular weight and are readily oxidized, and so agree with these generalizations.

5.11. Hormones in Invertebrates

Until 1928 no clear case of the existence of a hormone in an invertebrate was known, but in that year it was shown that contraction of the chromatophores of the shrimp is caused by a substance formed in the eye-stalks. This is now known to be general for those Crustacea which can change colour, and in one species two hormones are known; the subject is more fully treated on pp. 167-8.

More recently hormones have been discovered in insects. The best known are the moulting hormones of the bug *Rhodnius*. The most probable scheme of their action is as follows, but there are other possible interpretations. During the first four nymphal stadia two hormones are produced. The first, which is probably formed in the part of the brain called the pars intercerebralis, is an imaginal hormone which initiates cell division and ecdysis. It is formed seven days after the single meal which is taken by the instar, and the stretching of the cuticle is apparently the stimulus. If a bug is beheaded within seven days after the meal, it does not moult, but is otherwise little affected, for it may live for twelve months; insects beheaded eight days after taking food moult at the normal time. The second hormone, probably formed in the corpora allata, stimulates nymphal development, and particularly inhibits the action of the first. When it is present moulting can occur but metamorphosis cannot, so that the adult insect is only formed after the fifth instar when it is not present. These hormones are not specific, and similar ones are known in Lepidoptera, Diptera, and Phasmidae.

Other hormones control the migration of eye pigments in Crustacea, and the chromatophores of cephalopods.

5.12. Hormones in Vertebrates

In vertebrates many endocrine glands and many hormones are known, their interrelationships with each other and with the nervous system being often very complex. Some of them, notably the thyroid, are concerned not with the stimulation of specific effectors, but with the metabolism of the whole or a part of the body. A list of them, with a brief account of their properties, follows.

5.121. The Mucosa of the Gut

The action of this in co-ordinating secretion by the digestive glands is described on pp. 26-7. In addition, an

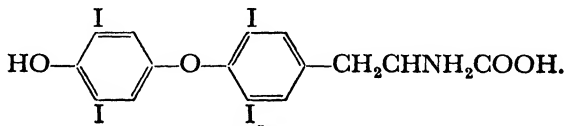
extract of duodenal mucosa activates the pancreas to produce insulin; the hormone concerned is not known, but it is not secretin.

5.122. The Pancreas

The islets of Langerhans in this gland produce a hormone called insulin which lowers the concentration of sugar in the blood. Its activity is described in section 1.43.

5.123. The Thyroid

The mammalian thyroid consists of two masses lying one on each side of the trachea just behind the thyroid cartilage. The division into two parts is secondary, and in the rabbit and many other animals the two halves are joined by a ventral strand across the trachea. The gland starts as a single diverticulum from the pharynx, and its position and mode of development show that it is homologous with the endostyle of *Branchiostoma* and lampreys. It is made up of closed vesicles with a wall of cubical epithelium. In the frog the thyroid consists of a small reddish body on each external jugular vein, and in the dogfish of a pear-shaped structure just below the fork of the ventral aorta. All the known physiological actions of thyroid extract can be brought about by thyroxine, which has been extracted from the gland and which has been synthesized. Its formula is



It has not been detected in the blood, and it is unlikely that it is actually the specific substance liberated by the gland, for gland extracts two or three times as powerful as thyroxine have been produced. It may be presumed, however, that something very similar to it is the essential internal secretion of the thyroid; in the gland it always

occurs combined with protein as thyreoglobulin. It is unique among hormones in that it is not easily digested, and so can be successfully administered by the mouth.

Over-activity of the gland produces the disease known as exophthalmic goitre, and under-activity myxoedema in adults and cretinism in children, but an account of these belongs to pathology rather than physiology. Their symptoms, however, suggest that the chief normal function of the thyroid is probably the regulation of the growth and activity of the animal. In particular it controls basal metabolism (p. 5), which in myxoedema may be 25 per cent. below normal and in goitre 100 per cent. up. The rise of temperature and increased metabolism in fevers are possibly caused by over-secretion by the thyroid, and it may be that the increased metabolism produced by low temperatures is brought about in the same way. The latter is the only case where it is likely that the thyroid normally varies in its activity during life so as to co-ordinate any other processes in the body. For the rest, it maintains a general control over certain aspects of metabolism, and is particularly important during the time when growth is going on; for example, the bones of cretins cease growing at an early age, and their mental powers never develop.

The thyroid also controls the metamorphosis of Amphibia, for if it be extirpated in tadpoles they grow far beyond their normal size and never change into frogs or newts as they should. Thyroxin, or even elemental iodine, will make such thyroidectomized tadpoles develop normally. Conversely, feeding normal tadpoles with thyroid makes them metamorphose at an early age—at six weeks instead of three years in the extreme case of *Rana catesbiana*—and the axolotl larva of *Amblystoma tigrinum*, which normally never metamorphoses, can be induced to do so. This activity of the thyroid is only brought into play by a secretion from the anterior pituitary.

5.124. The Parathyroids

The parathyroids lie on the surface of, or embedded in, the thyroid, and consist of two pairs of bodies derived from the third and fourth branchial pouches. Their secretion, which has not been obtained pure, is called parathormone or parathymin. Its action is obscure, but injection of it raises the level of calcium in the blood, lowers that of phosphate, and increases the excretion of both. It is natural, therefore, that abnormal activity of the gland should interfere with bone formation, and, since altering the ionic balance affects the muscle proteins and nervous system, that its removal should cause tetany. The exact way in which parathormone controls the calcium and phosphate metabolism is unknown, but it acts in a very different way from vitamin D (p. 52) for it splits up the calcium phosphate of bone. It has also been claimed that extract of parathyroid retards growth in rodents and Amphibia.

5.125. The Thymus

The thymus has long been suspected as an endocrine gland, but it is only recently that any good evidence for its action has been published. It consists in mammals of two masses in the space (the mediastinum) in front of the heart. They are derived from the epithelium of the gill slits. In the frog there is a small lobe at each angle of the jaw, and in the dogfish a small mass above each gill cleft. It is largest in young animals, and in man is at its maximum at two years, while at puberty only traces remain. This at once suggests that its function is connected with growth, and it has been found that if extract of thymus be injected into rats greatly accelerated development follows. In particular the time of descent of the testes or opening of the vagina (the sign of sexual maturity) was reached much earlier. This effect on the reproductive

organs has been confirmed on mice, but in these animals no general effect on growth was found.

5.126. The Pituitary

The pituitary is a complex gland in both origin and function. In mammals it consists of four parts, the pars

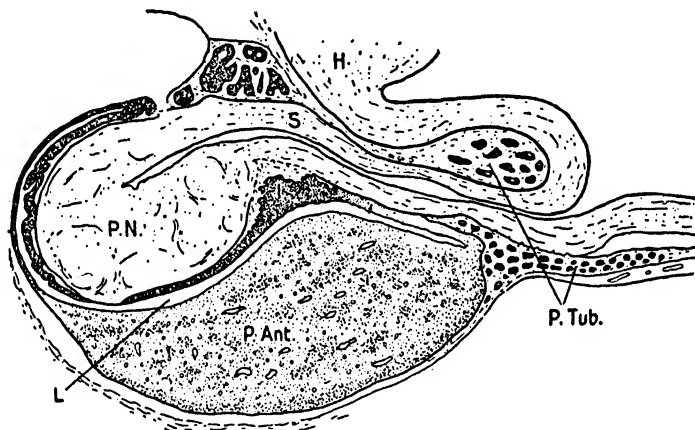


FIG. 31. Pituitary body of cat.

P. Ant., pars anterior; *P. Tub.*, pars tuberalis; *P.N.*, pars nervosa; *I.*, pars intermedia (darkly staining tissue enveloping *P.N.*); *L.*, cleft separating *P. Ant.* from *I.* (this is the residual lumen of Rathke's pouch); *S.*, stalk (infundibulum), showing cleft which is continuous with third ventricle; *H.*, hypothalamus. From a drawing by Dr. J. H. Woodger.

anterior, pars tuberalis, pars intermedia, and pars nervosa (Fig. 31). The first three are formed from the hypophysis, which is an upgrowth from the roof of the mouth homologous with the preoral pit of *Branchiostoma*. The pars nervosa is developed from the infundibulum, which grows down from the floor of the third ventricle. The pars anterior is known as the anterior lobe, in which the pars tuberalis is sometimes included; the other two make up the posterior or neuro-intermediate lobe. Each part has several functions and produces several secretions. A full

account of the activity of the pituitary has not yet been worked out, but the following is a minimum list of the hormones which it produces, and their functions.

The anterior lobe produces eight groups of secretions, of which the first is the growth hormone, phyone, which has a controlling effect on growth, particularly of bone, connective tissue, and epithelium. Excess of it leads to gigantism and the disease called acromegaly, in which hands, feet, and lower jaw are of unusual size: similarly a deficiency produces dwarfing. The thyrotropic hormone or θ -factor stimulates the thyroid to activity. Its apparent effects are therefore the same as those of excess of thyroxin. Tadpoles without an anterior lobe do not metamorphose, but they can be induced to do so by administration of iodine, so that the pituitary probably acts simply by stimulating the thyroid. Various experiments have shown that it works by controlling both the activities of the thyroid in manufacturing thyroxin, and the liberation of the latter into the blood. It is not clear that the thyrotropic factor and phyone are distinct substances. Adrenotropic hormone stimulates the suprarenal cortex. The gonadotropic hormones, which are active in the reproductive cycle, are described in section 7.22. The lactogenic hormone, prolactin, can initiate and maintain secretion of milk. The diabetogenic hormone affects the metabolism of carbohydrates, raising the blood-sugar by an unknown mechanism and inhibiting peripheral utilization of glucose. The ketogenic hormone causes an increased break-down of fats to ketone bodies, which appear in the blood and urine. It appears to lead to an increased storage of glycogen in the liver, which would presumably be due to saving of carbohydrate at the expense of fat. Lastly, the pars tuberalis produces a hormone called w substance, which causes the contraction of amphibian and elasmobranch melanophores (p. 171).

The posterior lobe is known to produce three hormones, the first two of which come from the pars nervosa. Oxytocin or α -hypophamine or pitocin stimulates the plain muscle of the uterus. It is used to assist in parturition. Vasopressin, β -hypophamine or pitressin, stimulates most other plain muscle in the body. As its first name implies, it causes rise of blood-pressure by constriction of the arteries. It is probably important in the maintenance of the normal tone of the capillaries. It, or possibly another hormone, causes an antidiuresis with retention of water in the blood even to the extent of diluting the plasma. Intermedin or B substance, which is formed particularly by the pars intermedia, causes expansion of the melanophores of lampreys, selachians, and amphibia.

5.127. The Suprarenals or Adrenals

The suprarenals or adrenals consist in mammals of two small bodies, one in front of each kidney. Each has two parts, an inner medulla and an outer cortex. The former, the suprarenal proper, is derived from the same set of cells as the sympathetic system, while the cortex has its origin in that part of the mesoblast which gives rise to the mesonephros. The functions of the two are quite distinct, and their association is probably an accident, for in some fishes they are quite separate. In the dogfish, for instance, the interrenal, representing the cortex, lies between the kidneys, and the suprarenals, representing the medulla, consist of small masses on the sympathetic chains. The adrenals of the frog lie on the ventral surface of the kidneys and are yellowish in colour. In some animals patches of tissue which is histologically similar to medulla or cortex are found detached from them.

Complete extirpation of the cortex causes death, which is accompanied by lowered concentration of sugar and sodium in the blood, and various other effects. There

has been prepared an extract of the tissue, cortin, or eucortone, which when injected will keep epinephrectomized animals (i.e. those from which the adrenals have been removed) alive indefinitely. It is therefore probable that the cortex produces hormones which are essential to life in that they assist in maintaining the normal functions of the body.

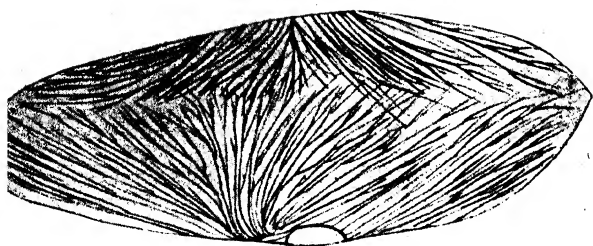
More is known about the medulla. It produces a substance, adrenalin, the formula of which is



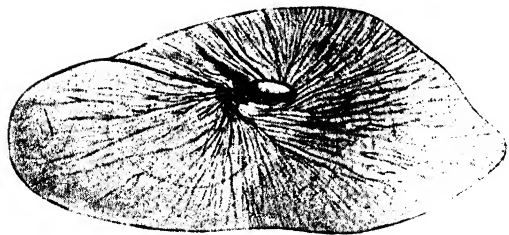
This, when injected into the blood, produces almost exactly the effects of stimulation of the sympathetic nervous system: it raises blood-pressure by arterial constriction; it causes contraction or relaxation of smooth muscle according to its origin and previous condition, dilatation of the pupil, erection of hairs by contraction of their muscles; it breaks down liver glycogen and muscle glycogen to lactic acid; it induces secretion of saliva; and in small doses it causes dilatation of capillaries. In addition it causes contraction of amphibian and reptilian chromatophores. Its exact function in the normal animal is obscure, but its most probable role is as follows. It is continually being produced in small amounts, but not in sufficient quantity to have any great effect. On the stimulation of cold, lack of oxygen, or the emotional states of fear and anger, its output is greatly increased, so that the characteristic effects of injection of adrenalin, which are also those of these emotions, follow. It is probable that the external stimuli act through the splanchnic nerves, which stimulate the medulla to discharge its secretion.

5.128. The Pineal

The pineal, which in the earliest vertebrates was an eye on the top of the head, is only a very doubtful endocrine gland. There are some clinical indications that it is concerned



b



a

FIG. 32. Neuromotor system of *Paramecium*: (*a*) oral view showing the oral whorl of fibres ramifying out from the neuromotor centre or motorium; (*b*) view of the left side, showing the ends of the fibres of both the oral and aboral whorls. After Rees.

with sexual development. Its extract causes contraction of anuran melanophores, but not of those of urodeles, and it does not appear to be normally important in this way.

5.129. The Gonads and Related Structures

The sexual hormones are described in section 7.22. It is still doubtful to what extent the interstitial cells of the gonads influence the secondary sexual characteristics, although there is a general impression that they do. It has recently been reported that the prostate in man and sheep contains a substance, prostaglandin, which stimulates plain muscle, and that of monkeys a substance, vesiglandin, which causes vasodilatation. These were not found in some other species of mammal which were tested.

5.2. Neuroid Transmission

Where there is no cellular structure there can be neither conduction by nerves nor conduction by fluids in blood-vessels. Where under such circumstances stimuli are nevertheless carried from one part of the cell to another their transmission is called neuroid. This name is also applied to conduction in cellular structures where no nerves or blood-vessels by which co-ordination could be effected are demonstrable. The word is little more than a name for our ignorance. There is well-defined conduction of impulses in the Protozoa; an amoeba, touched at its forward end, very soon starts forming pseudopodia at the opposite pole. In ciliates the co-ordination of the cilia is only maintained so long as the neuromotor system is intact (Fig. 32). When the fibres of this are cut the cilia beat at random. Similar fibres have been found in cells of ciliated epithelium, where the cilia are kept in a rhythm by conducted waves which do not necessarily travel in the same direction as the beat of the cilia (p. 122). The conduction of stimulus cannot therefore be mechanical. When sperms are allowed

to come together and clump, the beating of their tails may become synchronized; this suggests that neuroid transmission takes place by the gradual diffusion of secreted substances, for in this case there is not likely to be any protoplasmic continuity. The same explanation might account for the fact that the cells of a sponge react to a stimulus received as far as a centimetre away from them.

5.3. The Nervous System

From an evolutionary point of view the nerve net, such as is found in coelenterates and echinoderms, is the most primitive type of nervous system. Little, however, is known of its physiology, and it is more convenient to start with the nerve-cell as it is found in higher animals and particularly in vertebrates. The characteristic unit here is the reflex arc. One nerve-cell called a receptor picks up a stimulus, and as a result transmits an impulse along a sensory or afferent fibre to a synapse; this is a junction at which the impulse is transferred to another fibre, called motor or efferent, along which it is conveyed to the effector. By this mechanism it is possible for one effector to be specifically joined to one receptor. More usually the case is not quite so simple: intercalated between the sensory and motor neurones are one or more association or internuncial nerve-cells, and each synapse is a complex junction in which the afferent neurone is connected with more than one efferent, or vice versa. The effect of this is that while there is still localization of response, one small part of the body responding to a stimulus received on another small part, yet an effector can respond to impulses received from more than one receptor, and the same receptor can influence many effectors. Any aggregation of nervous tissue consisting of the synapses and adjacent parts of the nerve-cells, or of complete association neurones, is called a central nervous system. The remain-

ing parts of the nerve-cells, mostly collected together into nerves, constitute the peripheral system.

5.31. Propagation of the Nervous Impulse

A nerve may be stimulated by almost any sudden change in its environment—by pressure, by heating, or by the application of chemicals—but in life sensory nerves are usually particularly sensitive to one form of stimulus. That the impulse passed along the nerve is independent of the type of stimulus is suggested by a simple experiment. The right eye is shut, and turned as far to the left as possible, and the eyeball is then pressed sharply with the finger at the outer (temporal) corner of the lids. A flash of light is seen, apparently just above the nose. A little consideration will show that an object in this position would produce an image on the retina at about the spot where pressure has been applied, and the obvious explanation is that pressure and light both have the same effect on the retina, but that the brain is accustomed to appreciate all stimuli received there as light.

For experimental work electrical stimulation is always employed, on account of the ease with which it can be controlled and measured. After one impulse has passed there is a refractory period during which a second stimulus is ineffective: the period for the frog's sciatic nerve is about 1 msec. at 20° C. and longer at lower temperatures; in *Carcinus* it is 2 msec. After the absolute refractory period there is a relatively refractory one, and this is followed by a time in which the nerve is abnormally sensitive. Even if a stimulus be inadequate, it is still followed by a refractory period, so that if stimuli are very frequent and correctly spaced (about 1,000 per sec. in the frog) none but the first one has any effect. The immediate effect of an inadequate stimulus must be to make the nerve super-sensitive, for if another inadequate one follows within 0.5

msec. a response follows, so that there has been summation. The relationship between strength of stimulus and duration of application, and the conceptions of rheobase and chronaxie (p. 135) are the same for nerve as for muscle. The two tissues are similar also in that the make stimulus starts from the cathode, and in their other electrical relations. Cooling the nerve greatly increases its excitability, and it is found that the effect is entirely on the rheobase; the chronaxie, as with muscle, is actually increased. Excitation and conduction are only possible within certain limits of temperature, which depend on the animal. Frog nerve at 2° C. is very sensitive, but mammalian nerve is inactive below 5° C. It is found that the larger the chronaxie the smaller is the fibre size and the greater the velocity of conduction.

The impulse takes a certain time to travel along the nerve, and this is fairly readily demonstrable with an ordinary nerve-muscle preparation with a long piece of sciatic nerve. A tracing is obtained, first with the electrodes as near the muscle as possible, and then with them near the cut end of the nerve; the muscle is later in responding in the second case. More elaborate methods are necessary to get good values for the velocity of transmission in individual fibres. It is found that the larger the fibre the more rapidly it conducts, and that medullated fibres conduct more rapidly than non-medullated. In mammals the fastest fibres are those of the motor and some sensory nerves with a velocity of 100 metres per second, but there are others which range down to 0.3 m.p.s. A high value for the frog is 40 m.p.s., for Crustacea 15 m.p.s., and for the squid *Loligo* 22 m.p.s. The temperature coefficient for conduction is about 1.7. When the velocity of conduction is measured crudely for a whole nerve the value obtained is obviously that for the fastest fibres present.

The propagation of the nervous impulse is accompanied

by a wave of electrical change, each part in turn becoming negative to the rest. It is by means of this change that the rate of propagation is usually determined. It has been shown with the cathode-ray oscillograph that the wave which passes down such a nerve as the frog's sciatic is a complex one, and its peculiar shape is due to the fact that the nerve consists of a bundle of fibres which produce different potentials and in which the impulse travels at different rates. The tracing of a wave in a single fibre is difficult, and the properties of single fibres are therefore obtained in part by inference. The largest fibres produce the highest potential and conduct the wave at the highest rate—about 3,000 microvolts and 42 m.p.s. in the frog—and other fibres range down to $25\ \mu\text{V}$ and 0.3 m.p.s. The action potential and the conduction rate both vary approximately as the area of cross-section of the fibre, and as (in mammals) all fibres apparently become medullated when they reach a diameter of 1 or $2\ \mu$, non-medullated fibres are the slowest. Work on single fibres has shown that after the action potential or spike (so called because of its shape on the tracing) there is a negative after-potential (i.e. one of the same sign as the spike) which may be as high as $25\ \mu\text{V}$, and then a positive after-potential of not more than $10\ \mu\text{V}$. The negative after-potential corresponds to the supersensitive period, and the positive to the sub-normal period.

The quicker fibres are also the more easily stimulated, so that a weak shock given to the whole nerve produces a wave from which the slowly moving low potentials are missing. The threshold for a fibre varies from moment to moment, and the size of stimulus which excites in 50 per cent. of cases is taken as the official value. The induction shock given to a nerve may last for 0.04 msec., but response does not begin for up to 0.4 msec. This is not true latency, for if during this interval another shock of opposite sign

is put in, the nerve does not respond, which means that the first shock cannot have got through to the essential part of the nerve. If there is a period of true latency, that is a period during which the stimulus has been fully received but response has not begun, it is certainly less than 0.1 msec.

The electrical wave travels in both directions from the point of stimulation, and there is physiological evidence that this can be the case with ordinary stimulation during life: normally, however, nerve fibres are stimulated only at one end, so that they never get a chance to conduct in more than one direction; fibres are either sensory or motor. When a nerve is kept excited by continuous stimulation, as by pressure on the skin or light on the eye, it is found that a succession of separate waves is passing along it. The individual impulses are all of the same size, but the more powerful the stimulus the more frequent they are. The upper limit to the number which can pass in a second is determined by the refractory period. Experimentally, rates as high as 450 or more per sec. have been obtained, but the rates in life are normally lower, anything between 5 and 50 per sec. being a fair value for both sensory and motor nerve.

If a stretch of nerve be narcotized, the action potential is lowered as it passes along this, but when it emerges into the unharmed part of the nerve it rises to its normal value again. This implies that the energy for the nerve current is provided by the nerve itself. This agrees with what little is known of the chemistry and heat production of nerve. The general relations of nerve to oxygen are similar to those of muscle. Oxygen is absorbed, carbon dioxide is liberated, and the process is more rapid when the nerve is stimulated. In the absence of oxygen lactic acid accumulates, but when oxygen is admitted it is removed with increased usage of the gas. If a nerve be deprived of oxygen

for long, it loses its irritability, and the loss is more rapid if the nerve be repeatedly stimulated. Readmission of oxygen restores the sensitivity of the nerve. Stimulated nerve also produces ammonia and inorganic phosphate.

In oxygen, frog's nerve at rest gives off 7×10^{-5} calories per gm. per sec., and about one-quarter of this amount in nitrogen. When an action current passes along a nerve the heat production rises above normal in three phases. There is an initial heat of about 5×10^{-6} cal./gm./sec. followed by a short rapid-recovery heat of about the same size, and a delayed-recovery heat lasting for up to an hour and about thirty times as large as the initial heat. The delayed heat is associated with the after-potentials.

A brief theory to explain the electrical, chemical, and thermal changes is this: the nerve-fibre is covered by a polarized membrane, and the actual passage of the impulse is a wave of depolarization, which appears as the action-potential wave. Little energy is needed for this. Recovery consists in repolarizing the membranes, a process which means separating oppositely charged ions and so doing work and consuming oxygen to provide the energy. It seems that the surface at which the depolarization takes place is that which bounds the axis cylinder. The depolarization is accompanied by an increase in permeability, so that the nerve-fibre loses ions to its surroundings. In nerve from the crab *Maia* the chief of these outwandering ions is potassium, and a dilute solution of a potassium salt applied to a nerve makes it inexcitable. So does deprivation of oxygen, and this also causes leakage of potassium. All this suggests that depolarization really consists in the loss of potassium ions through a membrane which has been made abnormally permeable. During the time that the depolarization exists the nerve would naturally be refractory. All that can be said of the chemistry is that it cannot be similar to that of muscle, since

there is no evidence for increased production of lactic acid on stimulation, and the thermal phenomena do not fit the requirements of lactic acid anaerobiosis.

It has been suggested that the neurofibrils in the axon are important in the act of conduction, but there is evidence that this is not the case. It is possible in the nerves to the tentacle of *Carcinus* to remove the bodies of the nerve-cells, and so to interrupt the fibrils. Impulses are nevertheless still able to pass, which implies that the fibrils are not necessary for activity. This and similar experiments on vertebrates also show that the body of the neurone is not essential to its activity except in so far as it contains the nucleus, so that isolated parts of the axon sooner or later die. The same thing is shown by the activity of the ordinary nerve-muscle preparation, in which no nerve-cell body is present.

5.32. The Synapse and Nerve-muscle Junction

Although, as has been said above, the impulse in a nerve-fibre travels in both directions from its point of origin, stimuli in the animal only pass in one direction—from sense organ to effector. This must be because the impulse can pass across the junction from fibre to fibre (or from fibre to effector) in one direction only. The synapse or nerve-muscle junction acts like a valve, so that in the central nervous system it allows an impulse to pass from axon to dendrites, but not in the opposite direction. The synapse therefore appears to be an important part of the system.

Between the application of a stimulus to a nerve and the response of the effector, there is a distinct delay, the latent time. This may be made up of a number of parts: first, there is the latent period of the effector itself. Then there is the time taken for the impulse to be transferred from nerve to effector, which is easily measured by the difference

between the latent period for direct stimulation and that when the nerve is stimulated as close to the effector as possible. Thirdly, there is the time taken for the impulse to travel along the nerve, which can be calculated from the known rate of propagation of the wave and the length of nerve. When these three together are subtracted from the total latent time for a given reflex, there is obtained the reduced reflex time. It seems that this can only be the time taken for the impulse to pass the synapses involved in the reflex. When the leg of a frog was stimulated the reduced reflex time for the contraction of the gastrocnemius of the same side was found to be 8 msec., but for the contraction of the gastrocnemius of the opposite side it was 12 msec. The simple interpretation of this is that the crossed reflex added one more synaptic junction, so that the time for an impulse to pass a synapse is 4 msec., and two synapses are involved in the simple reflex. Of course, two extra synapses might be involved in the crossed reflex, in which case the time for one would be 2 msec., and four would be used in the simple reflex.

It is characteristic of the nervous system of the higher animals that there is localization of response, and this is not abolished by the interpolation of association neurones, for these merely allow one effector to be connected to more than one afferent nerve, and vice versa. In normal reflex action, for instance, a muscle may be caused to contract by stimuli received by several different sensory nerves. But when one such nerve is stimulated it will not cause anything like as great a tension in the muscle as direct stimulation of the motor nerve, a phenomenon termed fractionation. The interpretation of this is that the afferent nerve which has been stimulated is connected with only a limited number of the fibres which make up the muscle. When two afferent nerves are stimulated together the tension developed is usually less than the sum of the tensions

got by stimulating the two nerves separately. This phenomenon, known as occlusion, suggests that the group of muscle-fibres to which the first nerve is connected, to some extent overlaps that connected with the second. In other words, one effector unit (here a muscle-fibre) is connected, through the association neurones, to two nerve-cells.

The account of reflex action contained in the last paragraph does not seem to agree with what can be observed of the histological structure of the central nervous system. The cells have so many processes, and so many connexions with other cells, that it would be expected that an impulse entering at one point could spread to every cell in the central nervous system and so to every motor neurone. This condition, although never normal, is observed in animals poisoned with strychnine, for in this state a touch on the skin causes vigorous contraction of every muscle in the body. In the normal animal there must be some mechanism which prevents this and maintains localization, and it is probably to be found in the varying resistances of the synapses. In the normal animal the impulse must travel only along a few lines where the synaptic resistance is low. Increase in strength of the stimulus will cause the impulse to travel along more pathways and across other synapses, but it is only under the influence of strychnine that all synaptic resistances are broken down so that response is general and uncoordinated.

Although the frequent passage of impulses along a path leads to fatigue, a less frequent use of the pathway makes it easier for subsequent impulses to travel along it, so that a response may now be elicited by a smaller stimulus than formerly. This is known as facilitation, and is presumably brought about because use breaks down the resistance at a synapse. Facilitation has the important effect that a strong stimulus, which often affects the sense organs as would a volley of stimuli, may travel farther, and

cause a more vigorous reaction, than a weak one, because a number of impulses is sent along the nerve, and each of them weakens the synaptic resistance and aids the passage of its successor. This has been shown to be the case in crustacean muscle, and it is very important in the nerve net of coelenterates (see below).

A third characteristic of the synapse in addition to facilitation and resistance is its ability to block other synapses, the phenomenon known as inhibition. If two stimuli, which by themselves would produce two different reflex actions, are applied simultaneously, in general the response for only one of them is obtained. The passage of the one impulse increases the block on nearby synapses, so that the pathway for the second impulse is closed.

Both histologically and in its ease of fatigue and valve-like action the synapse resembles the nerve-muscle junction. It is probable that the two are physiologically very similar, and that in both the nervous impulse is transmitted by the liberation of a chemical substance.

A heart can be kept going for a long time with an artificial fluid circulating through it, and it is found that if such a perfused heart be depressed by stimulation of the vagus, and the perfusion liquid be passed through a second heart, the latter also is slowed. The obvious interpretation of this is that the vagus, in acting on the heart-muscle, liberates some substance into it. This substance has been identified as acetylcholine,



and there is abundant evidence that in vertebrates the voluntary nerves and the parasympathetic system act on their effectors by liberation of this base. Such nerves are said to be cholinergic. Most tissues contain an esterase which rapidly destroys acetylcholine, so that it does not accumulate. Stimulation of sympathetic nerves produces

a substance of unknown composition called sympathin, which acts in the same way. It is similar in most of its properties to adrenalin (p. 182), but is perhaps not identical with this. Nevertheless, nerves of this class are called

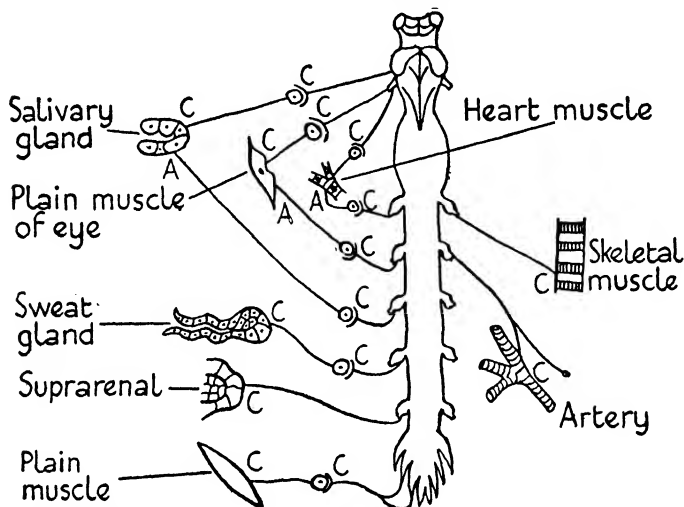


FIG. 33. Diagram showing points in the vertebrate nervous system where there is evidence of cholinergic transmission (C) and adrenergic transmission (A). On the left, sympathetic and parasympathetic fibres and their ganglia; on the right a motor fibre and a sensory fibre with a peripheral axon branch. Slightly modified from Dale.

adrenergic. The distribution of the two classes of nerve is shown in Fig. 33. The nerves which control the chromatophores of fishes are said to produce unidentified substances which are fat-soluble and slowly diffuse through the tissues to affect the colour cells. They have been called lipohumours to distinguish them from the water-soluble hydrohumours which include the hormones of the ductless glands and both sympathin and acetylcholine. Chromatophores are not modified muscles, but structures *sui generis*, and they appear to need special neurohumours to control them.

To what extent a similar explanation applies to invertebrate nerves is unknown, but annelids and crustacea appear to be similar to vertebrates.

It is easy to suppose that synaptic transmission is similar. The relaying of impulses in both sympathetic and parasympathetic ganglia is due to the liberation of acetylcholine, and it has been shown that other ganglia can produce it. If this be so, fatigue might be caused by a local exhaustion of the sources from which the neurohumour is produced; resistance is merely a measure of the time for an adequate concentration of the substance to be produced, and summation and facilitation are caused by successive formation of small amounts of it. The one-way conduction at the synapse would be due to the fact that the active substance could only be produced at the one end of the nerve, and for this there is some histological evidence. The giant fibres of annelids and Crustacea consist of chains of large cylindrical fibres which overlap one another, and the overlaps are called macrosynapses. The median fibre or fibres transmit only anteroposteriorly, and the laterals only in the opposite direction. In both cases the side of the synapse to which the nervous impulse comes first (the discharging side) stains more deeply with osmic acid than does the other, showing that there is a real chemical difference between the two. There are, however, some facts which do not easily fit in with this hypothesis, and some physiologists maintain that synaptic transmission, like that along a nerve-fibre, is essentially electrical.

5.33. The Central Nervous System

So far as it has been possible to study them, it has been found that the internuncial neurones of the central nervous system behave in a somewhat similar way to ordinary nerve-fibres, but they have their peculiarities. The duration of their positive after-potentials is much longer, and they are

able to lengthen or repeat the impulses which they receive. The impulse given to an internuncial neurone by an afferent nerve lasts for not more than 1 msec., but that which is received from the spinal cord by a motor neurone may be as long as 25 msec.

The grey matter of the central nervous system, which consists chiefly of cell bodies and synapses, is somewhat different in its metabolism from nerve-fibres. Its resting oxygen consumption is about five times as great, and it ceases to function normally as soon as the oxygen concentration falls below a certain value. At the same time it needs a continual supply of organic food, while nerve-fibres and muscles continue to live actively in plain Ringer solution, and go on using oxygen. The consumption of oxygen by grey matter begins to fall as soon as it is placed in Ringer, and can only be kept up if glucose or certain other substances be present in the perfusion fluid. In the living animal the case is similar, except that glucose, fructose (which is readily converted to glucose by the liver), and mannose are the only substances effective. These results imply that the central nervous system requires more energy than it can get by anaerobic respiration, and that it carries no reserves of substrate. It is not known to what part of the nerve-cell it is to which this chiefly applies, but it is possible, in view of their great importance, that it is the synapses.

5.34. The Nerve Net

The bare nature of a nerve net is adequately described by its name; it is a nervous system in which one cell connects with many others, so that localization seems impossible. It is the only type found in the coelenterates, makes up most of that of the echinoderms, and is found in some other places such as the small intestine of vertebrates and on the foot and labial palps of mussels. The central ner-

vous system of vertebrates is a network of nerve-cells, but differs from the others in that it consists almost entirely of association neurones which have no direct connexion with any effector or sense organ. The cells of the nerve net in the usual sense of the word supply both effectors and receptors, so that there are no motor or sensory nerves and no necessary connexion with the central nervous system. In coelenterates no central nervous system is present at all.

Most of the more recent work has been done on sea-anemones, and it is to these that the following account applies. The best histological work indicates that there is no direct connexion between two nerve-cells, so that the junction is a synapse just as it is in vertebrates. This means that there is no need to expect the behaviour of the net to be greatly different from that of an ordinary nervous system, and this is in fact the case. The nervous impulse travels with a finite velocity, but one which is much less than that for vertebrate nerve; for the general nerve net of *Calliactis* it is from 0.1 to 0.2 m.p.s. as compared with a minimum of 0.3 in the frog. But the values for the frog are those for the velocity in a single nerve-fibre, and, as has been pointed out above, a finite time appears to be taken for an impulse to pass each synapse. The nerve net contains very many synapses, and it is to be expected that the velocity of conduction in it would be slow. In some parts of the sea-anemone, such as the mesenteries, where there are specialized conducting tracts, it is over 1 m.p.s. In *Calliactis* the refractory period is from 40 to 60 msec. and the chronaxie from 2 to 4 msec.

In most cases the conduction is diffuse, with a complete absence of polarity. A stimulus applied at one point spreads equally in all directions, and reaches any other given point in the animal by the shortest possible path. Considerable cuts may be made in the tissue, and provided the nerve net still has any continuity the stimulus can reach

any part of the body. A jellyfish may be cut into a spiral strip, and the nervous impulse will travel right along it. The impulse apparently behaves like an electric current in a network, a result which is to be expected from the structure of the nerve net. There is no distinction of motor and sensory nerves, and stimuli can be transmitted in both directions across the nerve-cell junctions; the latter are therefore slightly different physiologically from the synapses of higher animals. In some places, for example on the tentacles of anemones, there is a certain amount of polarity, which appears to be of two sorts. Centripetally, that is from the tentacle into the mesentery, conduction is always much easier than anywhere else, which suggests that there is some anatomical peculiarity of the cells allowing this. Centrifugally, that is from mesentery to tentacle, the polarity is physiological; when repeated stimuli are given facilitation occurs much more readily in this direction than in any other. This presumably means that facilitation is easier in one direction across a nerve-junction than in the other—perhaps a forerunner of the coelomate synapse, which conducts in one way only.

In two important points the nerve net appears to be greatly different from a localized nervous system, but they can be satisfactorily explained in terms of the properties of all nervous tissue. As an impulse spreads out from its point of origin its response becomes weaker and weaker, so that there appears to be conduction with a decrement, which is quite unknown in ordinary nerve-fibres. Secondly, there is graded response; a light touch on a tentacle of *Hydra* will cause that tentacle alone to contract, a stronger will cause other tentacles to do so, and a very strong one will cause the whole animal to respond. These two phenomena are basically the same, and both can be explained in terms of facilitation. The usual stimulus, whether mechanical or not, is really compound, and consists of a

succession of impulses presumably relayed to the nervous system by the sense organs. A weak stimulus means a low frequency of impulses, a stronger one a higher frequency. The greater the frequency, up to a limit set by the refractory period, the easier will be facilitation. In most cases in anemones the important junction where facilitation takes place is that between nerve and muscle, but in some that between nerve-cells is involved. In both types a stronger stimulus activates more muscles or travels farther than a weak because it in reality consists of a more rapid succession of unitary impulses. The nature of facilitation is unknown, but its effect persists much longer at lower temperatures—three times as long for a fall of 10° C. This would be compatible with the suggestion made above that facilitation consists in the liberation of a chemical substance: the rate of destruction of this would naturally be lowered by a fall in temperature.

5.4. Mechanical Co-ordination

In the rhythmical movements of many segmented animals nervous co-ordination is assisted by a purely mechanical element. The ordinary locomotion of the earthworm is effected by alternate contraction of the circular and longitudinal muscles so that the body is alternately extended and contracted. The segments contract successively from the front backwards, and the resulting wave, assisted by a differential coefficient of friction in the two directions along the body, causes the body to move forward. If all the tissue but the nerve-cord be removed from one segment, locomotion can still continue, and the same is true if up to six adjacent segments are similarly treated. But if the nerve-cord be left as the sole connexion for a greater length than this, the part behind the operation becomes inactive. The nervous system alone is not adequate to co-ordinate movement. The explanation lies in the fact that

contraction of one segment causes a mechanical stretching of the next. This stimulates proprioceptors in the muscles of that segment, which send an impulse via the central nervous system back to the muscles to cause them to contract. The process is then repeated for the next segment. The central nervous system is thus necessary but by itself inadequate for co-ordination.

A similar explanation holds for the swimming of *Nereis* and of the eel and other fishes, as well as for the walking of Amphibia and probably of the dog. In all these cases the brain acts as an inhibitor of a locomotory rhythm which would otherwise continue unchecked. A *Nereis* without a head swims continuously because there is nothing to stop the rhythm, and if a decerebrate dog be suspended with its legs off the ground, the weight of its legs stretches the muscles and so causes the animal to perform running movements.

5.5. Sense Organs

It is a truism that an animal cannot respond to a stimulus unless the latter is first picked up by a receptor or, in more general language, a sense organ. On the subject of sensation, physiology becomes even more intimately connected with psychology than it does on behaviour, for strictly speaking all sensation is subjective. Nevertheless, some little is known about the means by which an event outside the animal becomes the starting-point for an event inside it, and it is with this that the present section is concerned.

The traditional statement that there are five senses is inadequate biologically for two reasons: first, even in man there are certainly more—the temperature sense is an obvious one left out of the usual list; secondly, and more important, the list is compiled not from observed reactions, but from subjective feelings which are not applicable to

animals other than man. An amoeba reacts to light, but it would be over-bold to conclude that it sees or has the sensation of sight. The rational way of dealing with sense organs is to classify them according to the type of stimulus to which they normally or chiefly react. It has been pointed out above (p. 185) that an isolated nerve can be stimulated in a number of ways, and the same applies to sense organs, the essential parts of which are in all higher animals made of specialized nervous tissue. But in spite of this, sense organs are often specialized so that they react particularly well to one type of stimulus, which is said to be adequate for them, and may be so shielded that other sorts do not normally reach them. For instance, the nerve-endings of the ear are so situated in the interior of the skull that only influences of vibration in a material substance and of acceleration can be transmitted to them.

In spite of all this it is difficult to get away from the subjective aspect of sensation. For it is found that the same stimulus, when received in man by different sense organs, produces different sensations. A striking example of this is given by a tuning-fork or piano wire of low frequency. The sensation it gives through the ear is that of a note appropriate to its rate of vibration, but if it be touched only a shaking feeling is obtained. The converse of this is also true, that however a sense organ is stimulated the same sensation is obtained. This is easily demonstrated by the experiment described on p. 185 in which pressure on the eyeball causes the sensation of light. The simple explanation of this is that pressure on the retina is interpreted as a source of light projected to a point such that it would give an image at the place stimulated. In other words sensation is a central phenomenon, and all impulses received by the brain from the same nerve-fibres are interpreted in the same general way. In reality this independence of stimulus and sensation provides further

justification for discarding the traditional list of senses in dealing with animals; we do not know what sensations an animal feels, but we can find out to what stimuli it reacts.

In many cases it is obvious without much experiment that an animal reacts to a stimulus, which must therefore have been picked up by a sense organ; when a paramecium meets some strange chemical in water and gives the avoiding reaction (p. 229) or when a dog lifts its leg and scratches its side where it is violently rubbed, there is clearly response. On the other hand, in those cases where a stimulus causes no sensible reaction, it cannot be assumed that the animal is incapable of reacting to it or that there is no change in the nervous system. The analogy from man is apposite: the effect of music on a listener is by no means proportional to his apparent reactions to it; the man who beats time with his foot will probably be missing much that is heard by a more educated listener who follows quietly with a score, although to an outsider the latter appears to be inattentive. Until recently, no method was available for finding out how far animals are sensitive to stimuli to which they do not appear to respond, but now there are two: electrical recording of nervous impulses, and the formation of conditioned reflexes (p. 241). It is obvious that a normally neutral or ineffective stimulus could not take the place of an effective one in eliciting a response unless the neutral stimulus were first received by some sense organ. By this means it has been found that vertebrates pick up many stimuli which are normally without apparent effect on them, but unfortunately the method has been little used with other animals. This procedure also enables one to test the power of an animal to discriminate between two similar stimuli. A dog, for instance, is trained to salivate to the sound of a tuning-fork or the sight of a circle, and is then tested with a fork of different frequency or with an ellipse.

Most sense organs respond over a fairly wide range of stimuli and discriminate to some extent between different intensities. It has been stated that the smallest perceptible increment of stimulus is, for a given sense organ, a constant fraction of the total intensity, a generalization which is known as Weber's Law. It would be safer to say merely that the larger the total stimulus, the greater must be any increase in it for it to be appreciated.

Many sense organs are continually exposed to stimulation and so send messages to the central nervous system quite apart from particular reflexes which they initiate; they are called stimulatory organs. Those which are most important in this respect are the proprioceptors, all statocysts (including the vertebrate labyrinth), the eyes of molluscs, arthropods, and vertebrates, and the halteres of Diptera. Destruction of any of these, or section of their nerves, causes loss of muscle tone, although there may be recovery after a time, probably because the stimulatory organs which are left intact become compensated for the loss of the others. Without some stimulatory organs, muscles appear to be unable to function properly.

5.51. Proprioceptors

In the muscles and tendons, and in the connective and skeletal tissues, are a number of sense organs which give rise to no well-defined sensation, but which, notwithstanding this, are of great importance. They are described histologically as muscle-spindles, Pacinian corpuscles, and so on, and the exact distribution of function between them is obscure. Collectively they are called proprioceptors, since they are concerned with stimuli which originate within the animal's own body, and they co-operate in the co-ordination of the position of the limbs. The sense with which they are concerned is called kinaesthetic. In man they permit the voluntary placing of a hand or foot in any

desired position. It is possible with the eyes shut to touch almost any part of the body with fair accuracy; the ability to do this has presumably been acquired by practice, with unconscious memory of the exact tensions and movements required to place the finger in the right spot. The proprioceptors are concerned with recording these tensions and displacements of the muscles. The same mechanism is used to a much higher degree in all cases of manipulative skill where the movement is one which has been learnt but which is now carried out unconsciously. Examples are found in piano-playing and skating. The statement, surprising or incredible to a beginner, that one should be able to drive a golf-ball blindfold, is correct because the movements of the body and limbs should be the same on every occasion, and with adequate training of proprioceptors this can be attained. From this point of view success at musical performance or games-playing or typewriting depends on a good proprioceptive mechanism. In learning all these things the eyes are used, but unless they can very early be put in a subordinate position progress is impossible.

In the appreciation of limb movement by the proprioceptors two things are important, the angular displacement and the angular velocity; the smaller the first, the greater must be the second for the movement to be felt. If the joints of the arm be considered in order from the shoulder down to the finger-tips, it is found that the sensitivity gradually decreases. This is of adaptive value in that a small angular displacement of a proximal joint of a limb means a big spatial movement of the distal parts.

In addition to making it possible for acts which were once voluntary to be carried out unconsciously, the proprioceptors assist in many reflexes which have never consciously been learnt. The most important of these are those by which the erect posture is maintained. The

human body is a very unstable structure, and it is only by continual adjustments of the muscles of the legs and trunk that man can stand upright. The eyes and ears help in this, but the proprioceptors are also important, particularly those which record the pressure on the soles of the feet. The ability to balance the body when one is skating or crossing a stream in the Lake District is acquired by modifying the normal reflexes through practice.

One particularly important action of the proprioceptors is in the maintenance of the stretch reflex. A muscle responds to passive stretching by an increase in its tone, which obviously counteracts the effect of the stretching. To a great extent this will account for the maintenance of posture. If the body begins to fall to the right, the muscles on the left will be stretched; their kinaesthetic end-organs will be stimulated so that contraction will occur and the body will be pulled back to its former position. The full explanation of the maintenance of posture, however, is much more complicated than this, other more intricate reflexes being involved.

Proprioceptive sense organs must presumably exist outside the vertebrates, but they seem to have been little studied. The receptors in the muscles of the worm which help to co-ordinate its movement (p. 199) are of this type, and small sense organs on the maxillary palp and legs of the cockroach have been shown to be tension receptors.

5.52. Tactile Organs

The skin of man contains many different types of sensory end-organs, but the allocation of these amongst the different types of sensation originating in the skin is difficult. Almost certainly, however, one of the endings concerned with touch is the fine nerve plexus which surrounds the base of each short hair. The sense organ is stimulated by its deformation, and the hair acts as a lever mounted at

its base, so that a force which would not be adequate to affect the nerve if applied directly may do so if it is applied at the end of the hair. The sensibility of the skin to touch is greatly diminished by shaving, but it is not abolished, and undoubtedly there are other tactile end-organs. The sensitivity may be investigated by exploring the surface with glass fibres of varying thickness. Each fibre bends at a particular pressure, which can be observed, and so can be made to press on the skin with its own constant pressure. By this means it has been shown that the sensitivity of the tongue and nose is twenty-four times that of the loins, and other parts of the body come between these extremes. Separate stimuli up to as many as 600 per sec. can be perceived as discrete.

In insects also, hair-like projections are important in the tactile sense. All over the body are fine hollow outgrowths of chitin, with a nerve-ending at the base of each of them. There are several different types, and some are probably connected with other senses.

Subjectively, man can distinguish pain from touch, though from the point of view of the stimulus, pain, as caused for instance by pressure from the point of a pin, is merely an increased touch. But pain can also be provoked by excessive stimulation of other sorts, high temperature for example, and, quite apart from the subjective side, it can be shown that different sense organs from those of touch are being used. Some regions of the body, such as the cornea, and internal organs like the intestine, are deficient in ordinary touch sense, but are very sensitive to deformation—the slightest depression of the cornea causes pain. In the condition of analgesia which occurs in certain diseases the pain sense is abolished but not the touch sense.

The physical difference between a pressure on an end-organ which causes pain and one which merely causes a feeling of touch is quite unknown, so that the distinction

remains a subjective one which cannot be applied to animals other than man. Probably all animals are sensitive to touch, and there is some evidence that some of them react violently to certain forms of it; this probably corresponds to the human pain sensation, for pain has no conceivable biological value unless it be the source of protective reactions. Tree-living caterpillars are continually being touched by the leaves and shaken by the wind, and give no apparent reaction, but quite a light touch of an unusual sort will cause them to drop down on their silken threads. The ordinary movements of the earthworm are controlled by the main part of the nerve-cord, but the convulsive movements which it makes when dropped into alcohol, stepped on, or otherwise strongly stimulated, are organized by the giant fibres. It is therefore likely that the two types of movement are started by different sorts of stimulus received by different types of sense organ. If violent or protective reactions to touch are said to be started by pain receptors, one must be careful to avoid any dogmatic assumptions of pain as a conscious state, for there can be no certainty of the existence of this in any animal other than man.

5.53. Temperature Organs

Some of the sense organs which occur in the skin are concerned with appreciating an alteration in temperature. It is probable that coldness and hotness are felt by different nerve-endings, but what exactly it is to which they respond is not clear. The fact that, if the right hand be placed in hot water and the left in cold, and then both be put into the same tepid water, the latter feels cold to the right and hot to the left hand, suggests that it is change of temperature—warmth is felt when the skin is warming up, cold when it is cooling. But after a hot or cold object has been placed against the skin and removed, its appropriate sensation

remains. In this case cold must be felt when the skin is warming up and vice versa. It is obvious that many animals are very sensitive to change of temperature and must therefore have sense organs associated with it. It has recently been shown that the ampullae of Lorenzini in the skin of elasmobranchs are receptors which continuously send impulses to the central nervous system. The frequency of these is increased by cooling and decreased by warming throughout the physiological range of the animals. In the region from 10° to 15° C. the organ in *Raja* is sensitive to a change of one-tenth of a centigrade degree.

5.54. Chemoreceptors

There is no particular reason why the same sense organ should react to all kinds of chemical stimulus, and the fact that different chemicals have different effects suggests that there is more than one sort of chemoreceptor, or organ sensitive to chemicals; in fact there are at least six in vertebrates. For animals living in water the only prerequisite for a substance to be able to stimulate in this way is that it must be soluble. For land animals it must also be soluble, but if it be merely that, it cannot be appreciated unless it has been dissolved in the saliva or in mucus on the skin. If, however, it be volatile as well, it may be appreciated from a distance. This leads to the existence in man of the two senses of smell and taste, of which the former may be very important since it is a projected sense by which the animal can react to distant parts of its environment.

The taste organs in man are the taste buds which are found in the stratified epithelium of the tongue and, to a lesser extent, in other parts of the buccal cavity. They are lemon-shaped bodies, made up of a few cells with nerve-endings between them. The sensory nerves are the lingual branch of the fifth cranial nerve, the chorda tympani branch of the seventh, and the ninth and tenth. Similar

taste buds are found in the oral cavity of other vertebrates, and in the Pisces some are found in other parts of the body as well. The catfish *Ameiurus* and a few other fish have them all over the body, and will turn and snap at meat or meat-juice placed in contact with the side of the animal.

Four primary taste sensations, sweet, sour or acid, bitter, and salt, can certainly be distinguished, and there are possibly two others, alkaline and metallic, as well. Other tastes are made up of mixtures of these, but a good deal of the apparent taste of foods is derived from their smell, as is clear when the effects of catarrh on one's enjoyment of a meal are considered. The simple experiment of holding the nose while eating shows the same thing. For these qualities derived partly from taste but chiefly from smell the name 'flavour' has been suggested. Different end-organs are concerned with the different primary tastes, for the sensitivity of different parts of the tongue varies from one to the other, and there are drugs which suppress one or two of them without affecting the rest.

In some way taste must be connected with chemical constitution: alcohols, sugars (which are polyhydric alcohols), and α -aminoacids are nearly all sweet, and so is the beryllium ion. Bitterness is produced by the ions of ammonium, magnesium, and calcium—it is noteworthy that these metals belong to the same group as beryllium—but chiefly by the alkaloids and some other organic substances. All compounds with three nitro groups are bitter and so usually are those with two, but one seems to have no effect on taste. Saltiness is characteristic of some anions: chloride is more potent than bromide, which is more potent than iodide. Sulphate and nitrate are also salty. Sourness seems to be exclusively connected with hydrion. The metallic and alkaline tastes, if they exist, are correlated with cations of heavy metals and with hydroxyl respectively. It has been pointed out that the four tastes are so

distinct that it is incorrect to speak of a single sense of taste. Why any substance should have a taste at all is unknown. There are a few compounds, such as dulcamarin, found in bittersweet, which definitely excite two tastes.

Most animals react by reflexes and taxes (section 6.2) to chemical stimuli, and any animal which takes food but rejects other solid particles—a discrimination possible even to *Amoeba*—may be loosely said to have a sense of taste. Butterflies and muscids have taste organs on the tarsi of the legs: the former respond by uncoiling the proboscis when their legs are brought into contact with apple-juice, and experiments showed that they could distinguish between sugar, acid, quinine (which is bitter), and salt. Under conditions of starvation one butterfly responded when its legs were stimulated by a solution of sugar only one-two-hundred-and-fiftieth of the strength of the weakest which can just be appreciated by man.

It might appear possible that chemical substances in high concentration might have an effect through their osmotic pressure. The gross effects caused by a change in this, such as are described in section 8.3, are hardly cases of response to stimuli, but it has been suggested that nematocysts respond to a lowering of the environmental osmotic pressure. In man, the mucous surfaces which are more or less exposed to the exterior—those of the nasal cavity, mouth, and larynx, the anus, and genital apertures—are sensitive to many chemicals. No taste is perceived, but the sensation is one of irritation, leading to such reflex actions as coughing and sneezing. The sense concerned is called the common chemical sense, and it is active only with relatively high concentrations of substances and leads usually to protective reflexes. The distribution of the sensitive endings is much the same in other land-living vertebrates as in man, but in Amphibia and fishes they

are found all over the skin. The endings are derived from the spinal nerves and, in the head, from the facial, and are distinct from those which are sensitive to touch.

In mammals the organs concerned with appreciating smells are nerve-cells with their bodies in the epithelium of the upper part of the nasal cavity, and the nerve connected with them is the first cranial. As has been pointed out above, land animals can only smell volatile substances, but mere traces of a compound are enough—mercaptan can be smelt at a concentration of 4×10^{-11} gm./litre. Even so, it is well known that the sense of smell in man is very poor compared with that in dogs and many other animals. The number of molecules which must enter the nose is, however, very large—about 2×10^{11} in the example just given. Most substances (other than gases) of strong odour have large molecules, so that their rate of diffusion is comparatively slow, but, as with taste, no explanation can be given for the possession of a smell by certain compounds and not others. Nothing useful is known about the analysis of smells, although several tentative schemes have been proposed.

The primates and seals have a poorly developed olfactory organ and are termed microsmatic. Most mammals are macrosmatic, and many of them are known to be very sensitive to smells. A few mammals, such as the toothed whales, have no olfactory organ and are termed anosmatic. Some sense of smell is shown by reptiles and birds, and both fish and Amphibia can find food at a distance when the nerves to the taste buds are cut, but not when the olfactory nerve is. They must therefore be able to smell, though for them the odorous substance need not be volatile.

The sense of smell is very important in insects; male moths find the females by characteristic scents which the latter emit. The sense organs are situated in the antennae, though it is possible that there may be a few in other parts

of the body as well. Bees are able to some extent to distinguish between odours, again by the antennae, and their discrimination is somewhat similar to that of man. *Trichogramma evanescens* is a chalcid parasite (Hymenoptera) which oviposits in the eggs of moths, and it distinguishes by smell between hosts which have been already parasitized and those which have not. It has been shown that there are at least two odours which it recognizes, one left by the feet of the previous chalcid and one arising from inside the parasitized egg. If parasitized eggs are washed, *Trichogramma* will pierce them with its ovipositor but will not lay eggs, so that it must be unable to recognize that the eggs are parasitized until it has pierced the shell. On the other hand, it will not oviposit on eggs which have been merely walked upon unless they have first been washed.

5.55. Organs of Balance

Many animals possess organs, which may be called generally statocysts, which enable their possessors to maintain a constant or given position with respect to the centre of the earth. The principle involved in all these is simple: a closed or nearly closed space has sensory endings on its inner surface, and contains particles of a higher specific gravity than the medium which surrounds them. Unless these particles are resting in one particular place they stimulate nerve-endings and so start reflexes which cause the animal to turn until the particles fall into their equilibrium position and the sense cells are no longer stimulated. The animal is thus able to orientate itself to the direction of the force of gravity. It is obvious that other forces might be able to move the particles; experimentally, centrifugal force can be substituted for gravity, and any sudden acceleration of the animal's body is sufficient to cause a reaction.

In vertebrates, the organ of balance is the pars superior

of the labyrinth (or of the 'ear'), consisting of the semi-circular canals and the utricle (Fig. 34). For all these

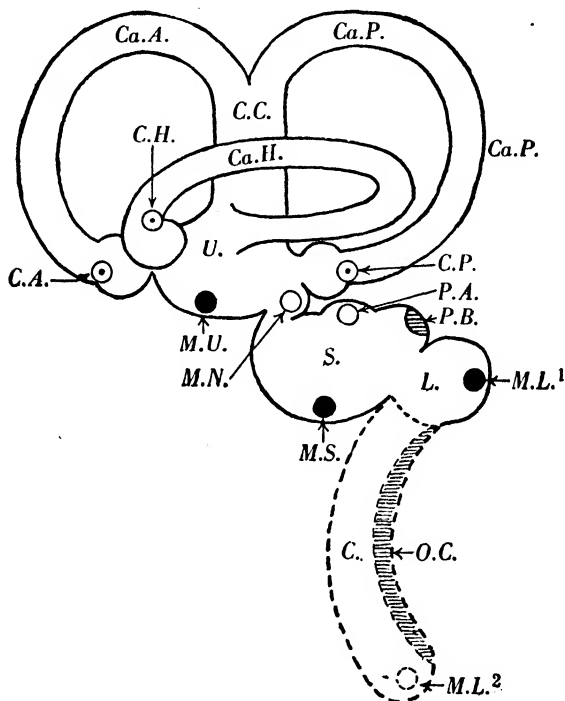


FIG. 34. Diagrammatic combination of the characters of the membranous labyrinth in all vertebrate classes.

C., cochlea; *C.A.*, crista anterior; *C.H.*, crista horizontalis; *C.P.*, crista posterior; *C.C.*, crus commune; *Ca.A.*, canalis anterior; *Ca.H.*, canalis horizontalis; *Ca.P.*, canalis posterior; *L.*, lagena; *M.L.*¹, macula lagenae in fishes and Amphibia; *M.L.*², macula lagenae in reptiles and birds; *M.N.*, macula neglecta or papilla neglecta; *M.S.*, macula sacculi; *M.U.*, macula utriculi; *O.C.*, organ of Corti; *P.A.*, papilla amphibiorum; *P.B.*, papilla basilaris; *S.*, sacculus; *U.*, utricle. The ductus endolymphaticus is omitted for the sake of clarity. After Löwenstein.

parts there is a bony cavity enclosing a membranous one; the latter contains endolymph, and between the membrane and the walls of the bony labyrinth is perilymph. On the inner surface of the ampulla of each canal is a

sensory ending called a crista ampullaris, and the utriculus bears a similar structure called a macula. All these sense organs are supplied by the eighth cranial nerve. The details of their arrangement differ somewhat in the different classes of vertebrates, but their general arrangement, and probably their physiology, are similar.

They enable the animal to react to gravity in such a way as to right itself, or, if this is physically impossible, at least to counteract to some extent the way in which it is held or the inclination of the ground on which it is standing. A frog, for instance, placed facing downwards on a slope, stretches out its forelegs in front of it and raises its head, thus bringing itself as nearly as possible into the ordinary position. The traditional case of an animal reacting to gravity is the cat, which falls on its feet no matter in what position it is dropped. Stimulation of its labyrinth, caused by its being in any but the vertical position in the air, produces muscular movements which rotate it until its feet are below and it is in equilibrium. The physical principles on which this is based are simple: first, Newton's Third Law of Motion, that action and reaction are equal and opposite, and secondly that the moment of inertia of a body depends on its radius as well as its mass. Suppose that the cat is held supine and dropped, and that its head inclines slightly to its right. It stretches out its hind legs, draws up its front legs, and twists the front part of its body to the right; by Newton's third law the hind part of the body must also rotate in the opposite direction, but it will not go so far to the left as the front part does to the right, because the hind legs are stretched out and the moment of inertia is therefore high. The cat then draws in its hind legs, stretches out its front ones, and twists to the left; this time, for the same reasons as before, the front part moves less than the hind part, and also moves less than it did at the first turn; the final result of the two twists is that the

cat's ventral side has been turned towards the ground. The labyrinth is responsible for some other special reflexes, such as the one by which a duck ceases to breathe when it dives. Pointing the bill downwards stimulates the labyrinth so that respiratory movements cease.

Corresponding reactions to both angular and linear accelerations have been shown to occur in all vertebrate classes except reptiles. The resulting muscular movements largely consist in rotations of the eyes, but there are also movements of the head and limbs, the latter, when stimulated by a downward acceleration, sometimes moving in such a way as to prepare for landing.

The distribution of these functions amongst the various parts of the labyrinth is obscure, and not necessarily the same in all the vertebrate classes, but in general the ordinary static reactions to gravity and those to rapid linear acceleration are controlled by the macula utriculi, while the semicircular canals are concerned with angular accelerations. The canals have a much smaller reaction time than the utricle. Practically nothing is known as to the way in which the stimulus is actually received, but it is probably due to movement of the endolymph. Since the labyrinth is the organ which chiefly determines the position of the body, it has been called the organ of the sense of space. It seems true that our ideas of space are derived from the perceptions of the labyrinth, but the further suggestion, that we conceive of space as having three dimensions because we have three semicircular canals, is not certain.

Some of the Protozoa, such as *Paramecium*, react to gravity, and so presumably possess some form of acceleration receptor. Statocysts are common in the coelenterates. In the Arthropoda they are invaginations from the external surface lined with chitin, and in the Crustacea the particles they contain are grains of sand acquired from outside

at ecdysis. If a moulting prawn is provided only with iron powder instead of sand it must of necessity use this to fill its statocyst, and after this has happened it can be forced to swim on its back by holding a magnet above it.

5.56. Sound Receptors

The pars inferior of the labyrinth of vertebrates (Fig. 34), consisting of the sacculus and the lagena and cochlea derived from it, is concerned with the reception of sound. In most of the mammals there is a more or less trumpet-shaped pinna which collects sound waves and concentrates them to the opening of the external auditory meatus. Moreover, it can be moved by muscles and so used to locate approximately the direction from which sound is coming. In man it is probably functionless. At the inner end of the external auditory meatus is the tympanum, a stretched membrane which is set into vibration by the waves which strike it. Its movements are imparted to a chain of three ossicles, the malleus, incus, and stapes, which stretch across the middle ear. The base of the stapes is sealed by a membrane into an opening, the fenestra ovalis, in the cochlea. The ossicles are so hinged on one another that the movement of the tympanum is accurately transmitted to this membrane. Variations in pressure in the air are therefore transmitted to the cochlea. The ossicles, under appropriate experimental conditions, can be seen to move, and in rabbits and dogs it has been shown that their movements are to some extent reflexly reduced on receipt of a loud sound, by muscles attached to the malleus and incus. There is thus a certain amount of automatic volume-control. The Eustachian canal, which leads from the cavity of the middle ear to the pharynx, prevents excessive differences of pressure on the two sides of the tympanum.

The cochlea (Fig. 35) consists of a tube wound helically

round an axis of bone called the modiolus. In this runs the eighth (auditory) nerve, from which branches are given off to the sense cells. The tube of the cochlea is divided longitudinally into three, by two membranes running along its length; apically Reissner's, and basally the basilar.

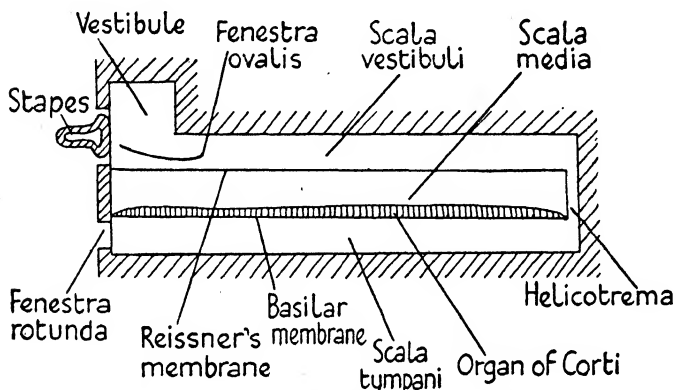


FIG. 35. A very diagrammatic representation of the mammalian cochlea, unwound. Diagonal shading indicates bone. The stapes is in the middle ear, and the fenestra rotunda also looks into this space.

The uppermost subdivision of the tube thus formed is called the scala vestibuli, and the lowest the scala tympani. These two contain perilymph and are in communication at the inner end by a small opening, the helicotrema. At the other end the scala vestibuli opens into the vestibule, in which the fenestra ovalis is an opening. The scala tympani has an opening, the fenestra rotunda, which is separated only by membrane from the cavity of the middle ear. The third division of the cochlea, between the two membranes, is filled with endolymph and is called the scala media. On the side of the basilar membrane which is bounded by endolymph is a series of hair-like sense cells, derived from the eighth nerve, which collectively make the organ of Corti, the essential organ of hearing. When the

base of the stapes is pushed inwards, the resulting increase of pressure moves Reissner's and the basilar membrane downwards, and the membrane of the fenestra rotunda bulges outwards to compensate for this. Vibrations of the ear-drum are thus transmitted to the organ of Corti.

The best-supported theory of the way in which sounds of different pitch can be distinguished is the resonance theory. It is now almost certain that the organ of Corti, although it appears as a continuous structure, is, in effect, a series of resonators, comparable to the strings of a piano. When one note strikes the ear only a very limited part of the organ responds. The resonators are arranged in order, with those for high notes at the basal end. This explains why it is possible for a man to become deaf for a very limited region of the sound spectrum. By using a very fine drill to damage the organ of Corti in a guinea-pig it is possible to produce deafness for one or two tones only, and so to map out the parts of the cochlea which are concerned with different notes.

The ability of the ear to appreciate small sounds depends on their frequency; the human ear is most sensitive to notes of about 2,000 cycles per second (roughly the third C above middle C—usually the highest but one on a piano). Frequencies from about 40 to 40,000 cycles/sec. can be detected, and over the middle part of this range, from 500 to 4,000, people who have not been specially trained can detect differences of three parts per thousand, or about one-twentieth of a semitone. With two notes so close together as this, however, only a person with a trained musical ear can decide which is the higher.

The direction from which a continuous sound comes is determined by the phase difference between the images obtained by the right and left ears, which depends on the different distances which the sound has to travel to reach the two ear-drums. For sounds of high pitch (more than

800 cycles/sec.) and therefore of short wave-length the same phase difference will be given with more than one angle of the incident sound (for a phase difference of $1+\alpha$ is the same as one of α) so that multiple images will be formed. Hence it is difficult to detect the direction from which a high-pitched note comes, and a very high note, such as the chirp of a cricket, seems to come from every side at once.

In all mammals the general mechanism of hearing is the same. Dogs can certainly detect differences of a semitone, and possibly of less, and have a memory for absolute pitch better than that of most men. Aquatic mammals possess various devices suitable to their special environment.

In other vertebrates the ear is more simple: there is no pinna; the external auditory meatus is short in Sauropsida and absent in Ichthyopsida; the middle ear of Amphibia, reptiles, and birds contains only one bone, the columella auris, which corresponds morphologically to the stapes, and in fish there is no middle ear.

Birds have a definite cochlea, not so well developed as that of mammals. It is evident from their powers of imitation that their sense of hearing is very good, and this is borne out by experiment.

Reptiles have a small cochlea, and lizards seem fairly sensitive to sound. Chelonians are apparently unresponsive, but sounds up to about 300 cycles/sec. cause impulses to pass along the auditory nerve; the sensitivity of the ear of the alligator is very similar, and in both, the threshold for stimulation is lowest at about 100 cycles/sec. Snakes have no tympanum and have the columella attached to the quadrate; they cannot hear air-borne sounds, but they can hear those which reach the skull directly from the ground. In Amphibia the cochlea is represented only by the lagena, a small projection on the sacculus. Frogs can be shown to respond to tones of from 50 to 10,000 cycles/sec.,

and there is some evidence that they can appreciate differences of frequency up to 500 cycles/sec.

Fishes have no cochlea, but the macula of the sacculus is an auditory organ. The hearing of fish has been investigated by the method of the conditioned reflex. Most marine fishes can be taught to respond only to low-frequency tones and many are quite deaf, but some fresh-water fishes are sensitive to frequencies of a few thousands, and can distinguish an interval of less than an octave. This increased sensitivity may be correlated with the presence of Weber's ossicles, extending from the sacculus to the air-bladder. From an evolutionary point of view the lateral-line organs of fishes are undoubtedly connected with the labyrinth. They consist of canals containing fluid into which project hair-like sense cells, and the organ is stimulated by anything which moves the fluid and so bends the cells. There is a constant background of stimulation, and touch and pressure, slow currents of water, and vibrations of a frequency of about six cycles/sec., are specially effective in altering the rate at which impulses pass along the nerve. This sensitivity probably enables the fish to avoid rocks and to perceive the movements of other fish. In addition, the fluid is moved when the animal's own muscles are moved, so that the organ can act as a proprioceptor.

Outside the vertebrates, well-developed auditory organs are found only in the insects. Some grasshoppers and crickets (Orthoptera) possess a quite complicated organ in the tibia of each front leg; it consists essentially of a membrane which covers a series of sense cells. Grasshoppers respond to chirps made by other grasshoppers, and they will also respond to similar artificially produced notes of a range of frequency from 430 to 28,000 cycles/sec. A female cricket finds a male by flying in the direction from which the latter's chirp comes, and no other sense

than hearing is necessary so that she will answer a telephone call from him. If one of the female's ears is destroyed her sense of direction is impaired, but she can still find the male. Each organ is directional, and must respond not to pressure, but to either velocity or displacement, both of which are vector quantities. Different sounds are distinguished by variations in the wave-length of a low frequency modulation carried by the high frequency primary sound.

Somewhat similar organs are found in the abdomen of cicadas (Hemiptera), and on the abdomen or thorax of many moths (Lepidoptera). These have been shown to respond to sounds. Some caterpillars of the Lepidoptera respond to sounds, the receptors being the hairs on the anterior part of the body. Structures called chordotonol organs, similar to parts of the ears of grasshoppers but without the tympanum, are found on the halteres of Diptera, on the legs of ants (Hymenoptera), and on the antennae of most insects, but they are probably proprioceptors.

5.57. Light Receptors

The only part of the electromagnetic spectrum to which animals respond in any special way is a narrow band of about one octave, roughly corresponding to the region which is visible to man. A few animals—planarians and *Daphnia* for instance—react to long-wave ultra-violet light, and owls perhaps to infra-red, and there are considerable variations in the limits of the visible spectrum both between different vertebrate species and between individuals. While other radiations are absorbed, and may, as in the case of X- and γ -rays, have considerable effects, they do not cause any but generalized changes. Light-sensitive regions of the body are very widespread; even the Protozoa react to light, and in *Euglena* and some other forms there is a definite eye-spot, which is a carotin-containing part of the cell which is specially sensitive. Eye-spots also occur in

Metazoa, though here they are simple cellular structures. In *Lumbricus terrestris*, for instance, there are at the base of the epidermis certain light cells, each consisting of a transparent lens-like structure which concentrates light on to a nerve-ending.

It may be assumed for physical reasons that in all cases where a structure is sensitive to light, the latter is responsible for initiating a photochemical reaction, probably with production of some substance which acts on a nerve. It is noteworthy that in many eye-spots the characteristic pigment is a carotin, closely related chemically with the visual purple found in the eyes of mammals.

Despite the wide occurrence of light-sensitive cells in the animal kingdom, it is only in the molluscs, arthropods, and vertebrates that a true eye, capable of forming images, is found. Of these by far the best known is that of vertebrates, particularly of the mammals. It consists of a converging lens system, made up of the cornea, aqueous humour, and crystalline lens, which forms an image on the retina. Accommodation, that is, the exact focusing of an image on the retina whatever the distance of the object, is brought about in mammals by altering the radius of curvature of the lens. The latter is contained in an elastic capsule, which is held in position by the suspensory ligament. Were the lens free, it would, owing to the elasticity of its capsule, have its maximum curvature, and would therefore be suited for the vision of near objects, but in the eye the suspensory ligaments are pulling on it all round, and so stretch it that it is focused for distant objects. When the ciliary muscles contract they remove the tension of the suspensory ligaments, and the elastic capsule increases the curvature of the lens and adapts it for near vision. Other methods of accommodation are found in other vertebrates; in birds the curvature of the cornea is altered, and in fishes and Amphibia the lens is moved towards the retina.

The sensitive elements of the retina of man are of two sorts, rods and cones. The central part of the retina, the fovea centralis, where objects are normally focused, contains only cones, and as the distance from this increases, the proportion of rods increases, until, at the periphery, there are scarcely any cones. The periphery of the retina is nearly colour-blind, so that it looks as if cones are necessary for colour vision. Many animals, such as dogs, are colour-blind, and in some cases, for example the mouse, this is associated with lack of cones. Further, the periphery is much better at appreciating very faint light than is the fovea; a very faint star can often be seen only when one is looking not directly at it but slightly to one side. This suggests that the rods are concerned in appreciating low light intensities, that is, in twilight vision. The retina contains a pigment, visual purple, which is particularly associated with the rods. It undoubtedly plays an important part in vision; its curve of light absorption is almost identical with the curve of visual sensitivity for different wave-lengths. It is similar in structure to vitamin A and is bleached by light to products similar to the carotins and is re-formed in the dark. If an animal is insufficiently provided with vitamin A it cannot see in the twilight, that is, it is night-blind. These facts suggest that the mechanism of vision for light of low intensity is simple and is as follows: the visual purple is broken down by a photochemical reaction and the products so formed stimulate the rods. The eyes of birds seem to work in a similar way; the ability of owls to find mice in the dark is not due to a particularly efficient type of twilight vision, but to their sensitivity to infra-red rays which are emitted by the rodents.

Not all workers accept this simple account of the function of the rods, some experimenters regarding them merely as nerve-endings controlling the secretion of visual purple; according to this view, the break-down products

of this stimulate the cones, which are the only sensitive elements.

No satisfactory theory of colour vision exists, but the best is probably a modification of the Young-Helmholtz hypothesis, according to which each cone contains three pigments, one sensitive chiefly to each of the three fundamental colours.

The eyes of molluscs vary considerably in structure; those of the cephalopods are noteworthy for being very similar to the vertebrates.

The eyes of arthropods are of two sorts; ocelli, and compound or faceted eyes. The former are found in both the larvae and adults of insects, and most of them are probably no more than light-sensitive structures; some of the more complicated of them may form crude images.

The faceted eyes are characteristic of adults. Each is made up of a large number of elements called ommatidia, each of which has a refractive body called a cone (it has no relation to the vertebrate cones), and below this a nervous retinula. The ommatidia are separated from one another by pigment, so that only rays which are nearly parallel to the axis of the cone will pass right to its bottom. There is more than one sort of ommatidium, and in the types known as eucone and exocone the refractive index of the cone gradually decreases from the centre to the periphery. With this structure it is possible for a cone to form at its base a real erect image of an external object. Since the pigment and the great length of the cones relative to their radius prevents all but nearly parallel rays from reaching the retinulae, the effect of this optical system is to give a real erect image of an object placed outside the eye, each ommatidium focusing a small part of it. That this is how the eye works in the glow-worm *Lampyrus* can be shown under the microscope. This type of image is called an apposition image. When, as in dim light, the pigment is withdrawn,

there is, presumably, overlap, and a superposition image occurs. In the type of eye called pseudocone, a similar apposition image is formed, but the parts formed from separate ommatidia are not erect, so that the total image is made up of dots of light like a half-tone plate. The method of working of the last type of insect eye, known as acone, is obscure. Some of the simpler types of compound eye, with few ommatidia, seem to have no function but that of appreciating light for phototaxis.

Insects are not, in general, colour-blind. Bees, mosquitoes, and butterflies, representing three different orders, can all distinguish colours, but their range is not by any means the same as that of the human eye.

VI

BEHAVIOUR

THE subject of animal behaviour may be approached by several different routes, but the only one with which a text-book of physiology is concerned is that which starts from observed changes in the whole or a part of the organism. For the purposes of this chapter, behaviour means the reactions of effectors to stimuli, and the simplest piece of behaviour is the muscle twitch which has already been considered. When the animal is taken as a whole its reaction to a single external stimulus is usually complex, several muscles, glands, and other effectors acting together to give a co-ordinated response. It is these responses, and their relations to the appropriate sense organs and co-ordinating system, with which the physiologist may legitimately deal, his aim, as in other branches of his subject, being to state his results in the simplest possible terms of physics and chemistry. A subjective approach, which regards the animal as a lesser man capable of thinking, of starting reactions independently of external stimuli, and being conscious of its own activity, may have its place in biology, but is no direct concern of the physiologist. It is rightly called animal psychology, and uses, as far as possible, the methods of human psychology. The stress in what follows on the mechanistic aspect of animal behaviour therefore implies no disapproval of any other side of the question, but merely a strict delimitation of the subject-matter of this book.

6.1. Behaviour in the Protozoa

The Protozoa are best treated apart from the rest of the animal kingdom, because they are made up of protoplasm which is not divided into cells. As a consequence there can

be no cellular co-ordinating system, and although it is sometimes possible to recognize organelles which are specialized as effectors (e.g. cilia) or receptors (e.g. eyespots), they cannot be so easily studied as separate entities as can the muscles and sense organs of higher animals.

It is traditional to start with *Amoeba*, and even if this animal is the degenerate which most protozoologists now consider it, its behaviour is, in the words of Dobell, pleasingly simple. In contact with a surface it moves, by means of its pseudopodia, in an approximately straight line, though it has been stated that its actual path is a sine curve. Its method of locomotion is described in detail on p. 128. If the front end of the animal comes in contact with a solid object, the direction of flow of the protoplasm is altered to make an angle with that which it had before. If only a small part of the anterior end has been stimulated, the angle is small, and the effect is that the amoeba moves round the obstacle. If the obstruction is large so that contact is made over the whole of the ends of the advancing pseudopodia, the direction of flow turns through nearly 180° and the movement of the animal is practically reversed. In both cases the final result is that the obstacle is avoided. Such a reaction, in which the animal is forced to move away from the stimulus, is called a negative taxis. In this case it occurs because pseudopodium formation is inhibited in the stimulated region. *Amoeba* gives a similar response to other stimuli besides contact; for instance, it moves away from unduly hot water or any solution of unusual composition, and will travel down a beam of light away from the source, because pseudopodia form more freely on the side which is worse illuminated. If a pseudopodium comes into a spot of very intense light focused up through the culture, it is withdrawn: others are put out, come into the light, and are again withdrawn, and this goes on until there is sudden reversal of the direction of

streaming, and the animal moves away from the spot. The larger the area of pseudopodium which comes into the light, the fewer the number of contacts before reversal occurs. The light acts by changing plasmasol to plasmagel, and the same effect is produced when a large area is stimulated once as when a small part is stimulated several times. If the same amoeba be watched coming into spots of light on successive occasions, it is found that it learns by experience, for the number of contacts necessary for reversal progressively decreases.

Besides these negative reactions *Amoeba* has some positive ones. Sometimes when a pseudopodium comes in contact with a surface, instead of withdrawing it sticks to it, and the whole animal moves up to it. This happens particularly when the amoeba is freely suspended in water and not otherwise in contact with a solid object. The feeding reaction, in which two pseudopodia are put out to surround a particle, is another positive reaction. While an amoeba is feeding it does not give the response to a beam of light described above. This fact, and the two types of reaction to contact, show that the behaviour depends not only on the external stimuli, but also on the internal state of the animal. It reacts automatically, but it does so to the whole situation, and not to an isolated element in it.

Paramecium is an example of a protozoan which is much more active than *Amoeba*. It swims by means of its cilia, and its locomotion may be analysed into three parts. It moves forwards, because the cilia beat backward; it rotates to the left on its long axis, because they beat not directly backwards but slightly to the right; and it pivots round its posterior end towards the dorsal surface because the cilia on the ventral side (by the oral groove) beat more strongly than the dorsal ones. The last two partially counteract one another, because on account of the axial rotation the direction of pivoting is being continually changed. The

total result is that the animal moves along a solenoidal course, rotating on its axis as it goes. The three factors, forward speed, rate of rotation, and diameter of the solenoid, vary more or less independently as the beat of the cilia changes. The cilia in the oral groove, which are visibly different from the others, are not necessary for this peculiar type of locomotion, for it is given by fragments of paramecia which possess no oral groove. Such fragments also give the reaction described below. It follows that the ordinary movement and the variants produced in it by external stimuli are brought about by different types of beat of the uniform cilia which cover the body.

All unfavourable stimuli are met by the same response, an avoiding reaction or phobotaxis. The forward stroke of the cilia is reversed, and those on the left side strike towards the oral groove instead of away from it. All three factors in the locomotion are thereby affected—the animal moves backwards, its rotation is slowed, and the rolling round its posterior end towards the aboral side is increased: in extreme cases the rotation stops altogether and the animal swings round in a circle in a plane perpendicular to its previous direction of motion with its body as radius and its posterior end as centre. The phobotaxis is given when the anterior end receives a stimulus of touch, high or low temperature, strong light, or unusual chemical conditions. It lasts for a brief interval, less than a second, during which the paramecium has gone back about two lengths, and then normal movement is resumed. On account of the wide angle through which the body has been rolling it is unlikely that the line of motion will be the same as before, and the obstacle, spot of light, or whatever else it was that gave the stimulus, may be avoided. If it is not, another avoiding reaction is given, and a succession of them may lead to a complete reversal of the direction of movement. No special sensitive organelle is known in *Paramecium*, but

the avoiding reaction is not given when the posterior end is touched.

The avoiding reaction is almost the only method by which *Paramecium* can deal with strange situations. When it is given, as described above, because the anterior end receives a stimulus, it is generally protective in the sense that it enables the animal to avoid the source of the stimulus. But it is also given in general adverse conditions, and then has no value whatever. If the temperature of a culture of *Paramecium* be gradually raised, the rate of movement increases and at about 30° C. avoiding reactions begin, and are repeated very rapidly. The result is that there is little forward motion, but the animals dance backwards and forwards over short distances rather like particles in Brownian movement. After a time they may become acclimatized to the new temperature or they may die; in either case the phobotaxis ceases.

The avoiding reaction is also responsible for the chief positive behaviour of *Paramecium*. If a drop of very dilute acid be placed in the middle of a large drop of a culture of *Paramecium* on a slide and left for a little while, it will be found that all the animals have collected in the acid. More strictly, the acid diffuses out, so that there is a concentration gradient from the centre of the drop of culture to its edge; the paramecia collect in the middle part of the drop, so that they are above a certain concentration of hydrion. It appears as if they had been attracted to the acid, but this is not the case. Their swimming may be considered as random, and so sooner or later all of them enter the central parts of the drop of acid. It happens that they can do this without giving an avoiding reaction, but that when they are swimming down a hydrion gradient they do give it at a certain concentration. The acid diffuses out as a spherical shell, so that once a paramecium has entered the acid it cannot get out. The avoiding reaction will alter the

course of the paramecium, but its new direction will still bring it up against the shell somewhere else. It is as if all fell walkers had to turn back at meeting the 3,000-ft. contour when they met it going downhill, but not when going up: sooner or later (if they lived in England) they would all be trapped on Scafell, Helvellyn, or Skiddaw.

Paramecium has two definite positive reactions: sometimes on contact with a surface it does not give the avoiding reaction, but puts out trichocysts by which it anchors itself to the surface. This happens especially when it receives a contact stimulus on two sides, so that it tends to collect in this way in corners such as those between the glass walls of its container and the surface film of water. When two paramecia hit each other, one at least of them usually gives the avoiding reaction, but if they meet by their ventral surfaces, and if the animals are in an appropriate condition, they may stick together and undergo conjugation.

In all the free-swimming 'infusorians'—ciliates and flagellates—which have been investigated the chief reaction is a phototaxis similar in general principles to that of *Paramecium*. The details vary with the type of locomotion, but in all there is reversal or stoppage of movement and a turning to one side. In a few cases the avoiding reaction is adapted to orientate the animal with respect to the direction of the stimulus. This is illustrated by *Euglena*. If one part of a culture of this animal is illuminated and another not, all the individuals collect by the avoiding reaction either in the light or in the dark, according to the external conditions; they are behaving just like *Paramecium* collecting in an acid. But in addition to this they also orientate so that they swim either towards the source of light (usually when it is weak) or away from it (when it is strong). The probable mechanism of this is as follows. The convexity of the eye-spot is opaque, and the concavity is sensitive to light, so that as the animal rotates, unless it is facing directly

towards or away from the source of light, it is alternately exposed and shaded. This alternation of stimuli causes the avoiding reaction to be given until the eye-spot is uniformly illuminated. The stimuli then cease, and the animal continues on its course without further deviation.

6.2. The Metazoa: Taxes

In the Metazoa effector and receptor are nearly always separated spatially, connexion between them being maintained by the nervous system or by this system aided by hormones. From an elementary point of view the study of behaviour is the study of reflexes, for behaviour may be considered as made up of many individual reactions of organs such as muscles and glands, and these may all be stimulated through the nervous system. An animal may move towards the light, and with sufficient anatomical knowledge similar movement could be induced by electrical stimulation of the appropriate nerve-fibres. The particular reaction to each electric shock could be stated in the same terms as the frog jerks discussed in section 4.31. Studies which have been carried out on the development of behaviour in ontogeny suggest that behaviour patterns develop as wholes, and that their resolution into separate reflexes is artificial, but this does not mean that no useful results can be obtained from such an analysis. In any case the total behaviour is much more complicated than any single reflex, and it is consequently useful to study it as a whole as well as in its parts.

The response of an animal to a stimulus in such a way that the resulting movement has reference to the direction from which the stimulus comes used to be called a tropism. In strict usage this term is now restricted to the bending response of a fixed organism, and as most animals are motile it has little application in zoology. The term now used for a reaction of this sort in which the whole animal

moves is taxis (plural taxes). The particular type of taxis is shown by a prefix indicating the sort of stimulus concerned. Thus photo-, geo-, rheo-, chemo-, aero-, and thigmotaxis are reaction to light, gravity, a current, chemicals, air, and contact respectively. A taxis is positive when the animal moves towards the stimulus, negative when it moves away from it. The study of taxes is made difficult by the fact that the directions of two stimuli received by an animal may be such that their effects are opposite, and also by the fact that the effect of a stimulus is not a fixed one. It depends on the other stimuli which are being received and on the internal condition (and hence the past history) of the animal. Thus *Planaria alpina*, a turbellarian living in mountain streams, becomes positively rheotactic and swims upstream only when its reproductive organs are developing. When it has laid its eggs it becomes negatively rheotactic and moves down again. The eggs of the moth *Porthesia* are laid at the bottom of trees. The larvae are at first positively phototactic, and move up to the top of the tree, where they start feeding on the leaves. Food changes the sign of their reaction to light and they slowly move down, eating the leaves as they go. In dealing with taxes it is therefore essential that the exact conditions of the experiment should be stated, and the one stimulus carefully isolated.

Taxes may be held to describe a number of the ordinary pieces of behaviour in animals, particularly in invertebrates. The desire of the moth for the flame is proverbial, and the swarming of bees and many other insects is probably a phototaxis. Many fishes orientate themselves to face upstream and maintain their position relative to the bank. This is apparently rheotaxis, but it is in reality a special sort of phototaxis, for they are reacting to moving images of objects on the bank going past them. The blow-fly *Lucilia sericata* lays its eggs as a result of chemical stimuli

which it normally receives from putrefying material, but the natural conditions can be in part replaced by ammonium carbonate or other substances. Oviposition is here a kind of chemotaxis. The woodlouse *Porcellio scaber* collects in moist air largely because it gives a phototaxis on entering dry air, and so once it is in a damp situation it is trapped like *Paramecium* in an acid.

A taxis is essentially a forced movement, and in some cases taxes can be shown to be due to an altered muscle-tone on one side of the animal. It has been shown, for instance, in many insects that a reduced light intensity on one eye of the animal causes a decreased muscle-tone of the legs of the same side. For example, if the bug *Ranatra* be illuminated from one side, the legs of the bright side are bent, indicating a high tonus of the flexor muscles, while those of the darker side are extended (Fig. 36). The same result is obtained if one eye is covered with an opaque black varnish; the legs are flexed on the side of the normal eye, stretched on the side of the blackened eye. A normal insect under lateral illumination necessarily takes longer steps with the legs on the dark side than with the others, and so moves in a curve towards the source of light. When it has come to face the light it will be in equilibrium, the muscle-tone will be the same on both sides, and it will move straight forwards. In the same way when an insect with one blackened eye is illuminated from in front and starts to walk, as it normally would do, 'towards the light, it takes longer steps with the legs on the side where the eye is blackened than with those of the other side, and hence walks in circles.

When an animal which behaves in this way is placed under the influence of two sources of light, its behaviour can be predicted by simple physical methods. Each source of light has its own effect on the muscle-tone, depending on the intensity of illumination it gives at the sense organs.

This in turn depends on its own luminosity, the distance from it to the receptor, and the direction of incidence of the light. These are straightforward physical things which can be measured, and it is easy to calculate from them the

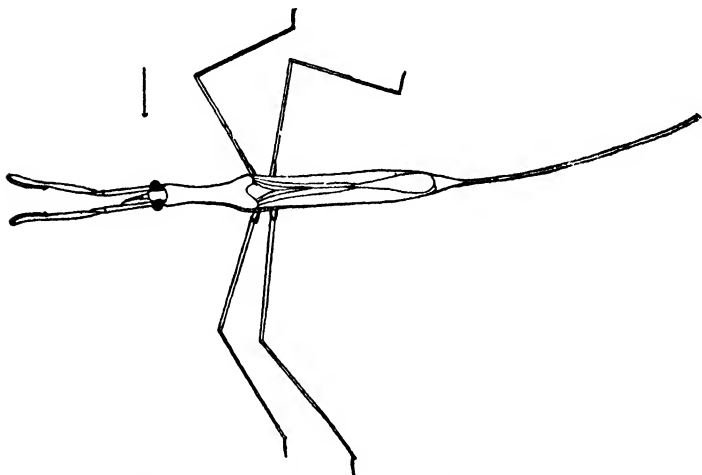


FIG. 36. Position of the water-scorpion *Ranatra* when the right eye is towards the light. After Holmes.

intensity and direction of a single lamp which would have the same effect as the two, that is, of their resultant. It would be expected that the animal would move towards the resultant, and this is found to be the case.

Such a forced movement, in which the direction-finding is due to an altered muscle-tonus, is called a tropotaxis. It is the type of behaviour originally described by Loeb under the name of tropism. It depends on the existence of stimulatory organs (see p. 203) which are easily influenced by outside stimuli. The tests for a tropotaxis, other than direct observation of muscle-tone, are that under the influence of two stimuli the animal moves along the resultant, and that where there are bilateral sense organs

extirpation of one of them causes circus movements. Animals react to other kinds of stimulus besides light in this way. Most of the cases where an animal orientates to gravity by means of a statocyst are of this sort, for unilateral extirpation of the sense organ causes rolling movements. Occasionally chemotaxis, movement towards a source of a diffusing chemical substance, is similar, as in *Planaria*, *Nereis*, and insects. In the case of the last the sense organs are in the antennae. When two stimuli of different sorts are acting on an animal, and its response to both is a tropotaxis, the two are compounded and the animal moves along the resultant just as it would if they were of the same sort. Thus the slug *Agriolimax* is both negatively phototactic and negatively geotactic. If it be placed on an inclined plane and illuminated from the side, it moves upwards at an acute angle away from the light.

As is normal with sensory stimuli there is some adaptation of these taxes, so that in the last experiment, for instance, the path of the slug becomes more and more nearly vertical, as it becomes adapted to the light.

There is another type of taxis, called a telotaxis, in which definite turning reflexes are given unless a sense organ receives the stimulus from a particular direction. This differs from a tropotaxis in two ways. When one lateral sense organ is extirpated there are no circus movements; the definite reflexes are still given until the animal is in equilibrium. With two stimuli the animal does not move along the resultant, but reacts to one only of them. In phototelotaxis, for instance, as shown by *Eupagurus*, the crab goes towards one of the two sources of light, and may suddenly change its direction and go towards the other. The recognition of tropotaxis and telotaxis as two distinct types of behaviour solves the problem of Buridan's ass, which could find no reason for going to one rather than the other of two similar bundles of hay at equal distances

from it. If it had reacted to hay by a tropotaxis, it would have walked midway between them and starved, but if by a telotaxis, it would have visited and eaten each in turn.

The crustacean *Leander* reacts to gravity by a telotaxis, and according to some authors it is the normal way by which insects orient in light.

The third type of taxis, the avoiding reaction or phobotaxis, in which the direction of the stimulus is only found by accident, has already been described for the Protozoa. It is not common in the Metazoa, but applies to the chemotaxis by which mites find their food and, as described above, to the way in which woodlice collect in damp air. The last is aided by the fact that the animals are less active in moist air than in dry, and this fact may by itself be sufficient to explain the local distribution of some animals. Earthworms, for instance, move actively if they are in situations which are dry and light, but are quiescent in those which are dark and damp, so that they collect in the latter.

6.3. Instincts

There are many cases where the reaction of an animal appears to be to a complex situation rather than to an elementary stimulus. Such responses are not called taxes or tropisms, but there seems no reason to regard them as being essentially different. For example, shrikes (butcherbirds) of the genus *Lanius* which have been reared in cages treat a piece of food which is given them in a peculiar way: they drag it after them until it becomes caught in a nail or some other projection, a piece of behaviour which agrees with the natural habit of the birds of impaling insects on thorns. Here the stimulus is 'food in the mouth', which cannot be reduced to light, temperature, or any other single factor, but the response is, nevertheless, as definite as is any taxis. The famous case of the pine processionary

caterpillar studied by Fabre is another example of this sort of thing. A caterpillar in the ordinary way will walk where its legs carry it, but as it goes it leaves a trail of silk behind it, and if a second caterpillar comes on to this it is bound to follow the first. The result of this is that the caterpillars move about in close single file, each one following its leader, and the processions are only broken by accidents which push an individual out of its path. Fabre was fortunate enough to induce a company of the caterpillars to make a closed circuit round the top rim of a large flower-pot. The march went on for seven days, interrupted only by pauses for sleep at night, and was finally broken by chance.

To such reactions as these the word instinct is generally applied, but many of the instincts of animals are much more complicated. They start with a piece of behaviour like those which have just been described, and then go on to several more acts in sequence, in such a way that the performance of one seems to act as the stimulus for the next. This is very well illustrated by the solitary wasps, which bury other insects and lay eggs in them. *Ammophila holosericea*, for instance, digs a hole in the earth, catches a caterpillar and stings it, then carries it into the hole, lays an egg in it, and finally closes the hole. This sequence is invariable, each act being the stimulus for the next. When a wasp was just about finishing closing the hole another stung and paralysed caterpillar was placed near by, and the wasp saw it. The sight of the caterpillar, the last part of the act of bringing a caterpillar to the hole, gave the impulse to bury, so the wasp reopened the tunnel. When she reached the bottom the sight of the egg and caterpillar already in position acted as stimulus for closing, so she carried on with this for the second time. But again she saw the caterpillar on the surface and again she reopened the hole, and then closed it for the third and last time.

A similar rhythm operates in the building of spiders' webs. *Araneus nauticus* is a species which makes a regular web similar to that of the common garden spider, *Epeira*

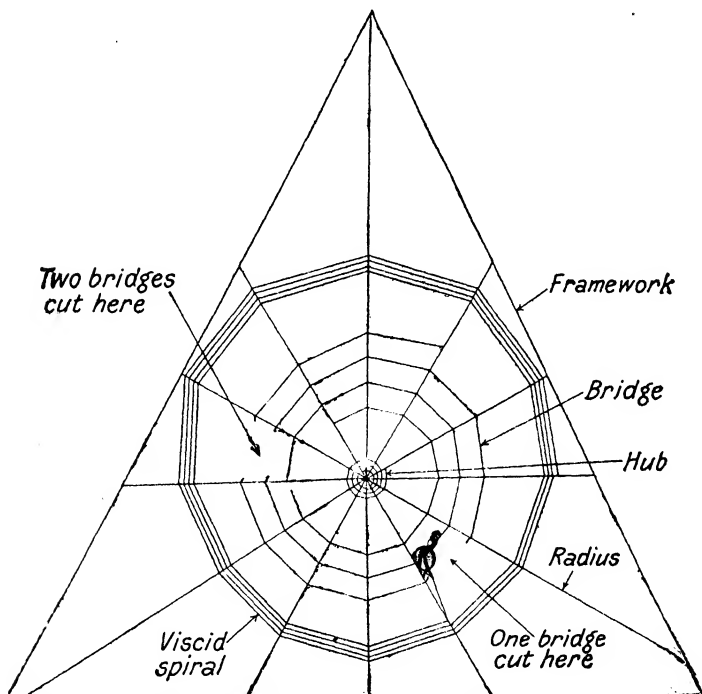


FIG. 37. Circular share of *Araneus nauticus*, showing how, after a bridge is cut, the spider cannot remake it, but crosses over by another bridge. After Hingston.

diademata. The web is constructed in five stages (Fig. 37) and the completion of each of the first four stages serves as a stimulus for the performance of the next. First, a framework is attached to surrounding plants, then a series of radii are taken from this into a centre; next comes a very close-wound spiral forming a hub round the centre, and fourthly the radii are joined by a series of bridges

formed by a spiral of fairly high pitch. All these parts are made of non-sticky silk, and are used as a framework not only to support the last stage but for the spider to walk on. The fifth stage is the viscid spiral, which is spun close together from without inwards; in order to make this the spider uses the bridges to cross from one radius to another. When a bridge is cut the spider does the best it can without it; it uses the next one, and so has farther to travel. Even if all the bridges in a sector are cut, so that the spider has to go right into the hub and out again, it is quite incapable of making a new bridge to save itself the journey. Even if all the bridges of all the sectors are cut no more are made. The spider goes on laying the viscid spiral, although now the framework is so weak that different radii come in contact and the result is a complete mess. Only the performance of one act, that of making the radii, can act as a stimulus for the making of the bridges.

This is analogous to a phenomenon common in learning repetition. We may know a poem perfectly by heart if we start at the beginning, but if we are asked to start at the third verse we may be helpless. Here saying one line acts as a stimulus for saying the next, and we can only find an individual line by going right through from the beginning. The two phenomena are, however, distinct, for the spider's behaviour is innate, whereas the other is learnt.

Instincts as defined in this way, that is complicated chain reflexes which are not learnt, are characteristic of the behaviour of insects. The notable thing about them is that they are subject to very little variation. Birds also are largely instinctive, but their behaviour is considerably modified by experience, and many things, such as a knowledge of suitable food, which in insects are possessed by an inherited instinct, in birds have to be learnt either by experience or from the parents. An insect feeds on the correct food plant, and can only with difficulty be induced

to feed on anything else: a chick will peck at anything which is moving or is otherwise conspicuous, and it is only after a time that it learns to restrict itself to food which is suitable.

6.4. The Conditioned Reflex

The formation of a conditioned reflex is the simplest type of learning, and accounts for much animal behaviour. An ordinary reflex, in which a muscle or gland reacts in a particular way to a stimulus, is inherited, but it is possible for new reflexes to be acquired by association during the life of the animal. The classical work on this was done by Pavlov on the salivary reflex of the dog, and a description of this will suitably explain the subject. A dog without previous training salivates when meat is present in its mouth. The strength of the reflex is conveniently taken as proportional to the amount of saliva produced. This is easily measured: a minor operation to bring the opening of one of the salivary glands on to the side of the neck is first performed, and a tube of standard bore is then attached to the opening. The rate at which drops of saliva fall off the end is an accurate measure of the rate of secretion. Almost simultaneously with the receipt of the meat by the dog the experimenter applies some other neutral stimulus, such as the sound of a tuning-fork, of which the animal normally takes no notice. The combination, food plus fork, is repeated a number of times, and then the fork is sounded alone: the dog salivates. A new, conditioned reflex has become established. For the formation of a conditioned reflex it is usually necessary that the neutral stimulus which is to become conditioned should be applied very shortly before the effective one. In some cases, however, conditioning has been possible to a stimulus which precedes the unconditioned one by a considerable time, and in a few cases to one which succeeds the unconditioned one.

Conditioning of strong or unusual stimuli is often difficult, and so is the transformation of an unconditioned stimulus for one reflex into a conditioned stimulus for another, but in certain cases these have been accomplished. Electrical stimulation of the foot, or pricking deeply enough to draw blood, which both normally lead to withdrawal of the affected part (and, by human standards, pain) have been conditioned as stimuli for the salivary reflex.

If there be applied, at the same time as the conditioned stimulus, a third strong stimulus, such as a flash of light, the response is not given; the new stimulus has upset whatever mechanism exists, and there is said to be external inhibition. The reflex can also be made to disappear in another way, by giving the conditioned stimulus many times without the unconditioned one. It becomes ineffective, and there is now said to be internal inhibition. In this case the mechanism of the conditioned reflex is still intact, for if the conditioned, but now ineffective, stimulus be given, and with it a flash of light, there is disinhibition—the conditioned response is given. The strong third stimulus has inhibited the internal inhibition. Inhibition can spread from one reflex to another. When one is internally inhibited, and the stimulus is continually applied, any other conditioned responses which the animal has formed are progressively lost, and the dog finally goes to sleep. Sleep is therefore regarded as a state of general inhibition.

The neural basis of the conditioned reflex is presumably facilitation in the central nervous system (p. 192). The two stimuli come together so frequently that the nervous impulse from the originally neutral one finally takes the path of the other, and so causes its response.

The formation of conditioned reflexes can be used to test the ability of an animal to distinguish stimuli. When a dog has been taught to salivate to a C fork, it will at first

do so also to any note anywhere near this. But if C is sounded and food given, and alternately a G fork is sounded and no food is given, it will learn to distinguish between them—it salivates to C but not to G. This must mean that the two notes can be distinguished by the ears. It is only a matter of experiment to find how far this discrimination will go.

Conditioned reflexes have been formed experimentally very widely in vertebrates, and in turbellarians, annelids, arthropods, and molluscs. The best-known experiments on invertebrates are those on bees. Incidentally these show that the stimulus can be a complicated one. The bees were trained to fly to a card bearing a pattern which had been associated with honey. It was found that solid black marks, whether triangles, circles, or squares, could not be distinguished apart. On the other hand, two concentric circles, triangles, or squares formed another group which could not be distinguished from one another, but which could be distinguished from the first group. The bees therefore react to a pattern, not to the shape of the figure.

It is probable that conditioned reflexes play a large part in the ordinary learning and behaviour of most Metazoa. The animal begins life with a limited number of inborn reflexes, but as it grows it forms new ones through the constant association of factors in the external environment. It has been said above that dogs salivate when meat is put into their mouths, and this is almost the only condition under which new-born puppies salivate at all. But, in general, dogs, and men too, learn very soon to salivate at the mere sight or smell of food, and it is a matter of common experience that this is the case. Without any special physiological experiments conditioned reflexes are formed because the taste stimulus of food is regularly preceded by smell and sight stimuli. The way in which it was long ago

shown that chicks learn to peck only at suitable food is by the formation of a conditioned reflex. At first they peck at anything moving or bright, but they very soon learn to avoid wasps and other objectionable things. When these are taken into the mouth their taste acts as an unconditioned stimulus for them to be ejected and avoided. In time the mere sight of them acts in the same way. The school of human psychology known as behaviourism seeks to explain all human behaviour as being built up by conditioning from a few simple reflexes.

6.5, Trial-and-error Learning

The last type of behaviour which will be considered here is learning by trial and error. The simplest case of this is that in which an animal has the choice of two exits from an enclosed space. One leads to a mild electric shock or some such nocuous stimulus, and the other to a reward of food and the comparative freedom of the normal living-quarters. There may be at first nothing to determine the animal to use one exit rather than another, and it takes the two indiscriminately, but in time it learns always to go to the one which leads to the reward. For clarity the two paths are generally distinguished in some definite way, as by a difference in illumination, but in some cases the animal can learn to go merely to its right or left. The design of the apparatus is varied to suit the animal—a glass Y-tube for worms, a tank of water for rats, and so on. Learning of this sort has been shown to occur in earthworms, in Crustacea, and in vertebrates. Whereas the worms need several hundred trials, crayfish need only fifty, and the higher mammals require only one or two. In the earthworm the nerve cord is involved, but not any special part of it. A worm which has learnt to find its way out can still do so when the cerebral lobes have been removed. In mammals it is chiefly the cerebral cortex which is used,

but, again, not any special part of it. If the posterior third of the cortex of a rat which has learnt its way out of a trap be destroyed, the animal no longer remembers how to escape, but it can learn to do so again.

This sort of thing has obvious similarities to the conditioned reflex, but it differs from it in that the learnt response has reference to a reward which comes after the response. There seems, however, to be no need to regard the two as being very different. If the animal goes on down the wrong path it receives a nocuous stimulus which would cause a retreat—this is an unconditioned reflex. In time the other things associated with this—bright light or turning to the left or whatever it may be—form a conditioned reflex, and the animal goes the other way. In the same fashion, the other exit, where it leads to a reward of food, takes the animal to a stimulus which would, by an unconditioned reflex, cause a positive reaction. Here also a conditioned reflex can be formed, and the particular conditions associated with the right exit act as a conditioned stimulus. A very small turning towards one or other of the exits may serve as a conditioned stimulus for the reaction normally produced by the reward or shock, as the case may be. Trial-and-error learning may then be said to consist in the formation of double conditioned reflexes, one positive and the other negative. It is true that the more complicated cases of trial-and-error learning, such as maze-running in rats, do not admit of such a simple explanation, but with them we leave physiology and enter psychology.

Trial-and-error learning is the basis of most of the behaviour of animals which is too complicated for explanation by inherited reflexes or simple conditioned ones. It is particularly concerned with cases where an animal is set a problem to solve, that is a situation which it has not met before.

VII

REPRODUCTION

WHATEVER may be the dictionary definition of reproduction, the word means in biology the production of an animal or plant which is in some way a different individual from the parent or parents which gave rise to it. An exact definition is difficult, but the general meaning of the word is simple. It is convenient and fairly logical to divide the methods of reproduction used by animals into sexual and asexual, but it must be noticed that the meaning of the second of these words does not correspond exactly with the use a botanist would make of the term; most of the asexual means of reproduction found in animals correspond more to the vegetative methods of propagation of plants than to the asexual method by means of spores.

7.1. Asexual Reproduction

Since there is less to be said about asexual reproduction than about sexual, it is convenient to take the former first, but it cannot be defined in any positive way. It is reproduction in which there is neither any sexual process, nor anything which can be interpreted as a reduced sexual process. It can take place in a number of ways, and the placing of these together under one head is probably more convenient than logical.

7.11. Fission

In its more restricted meaning fission implies the division of an energid, and consequently it can only be a method of reproduction in the Protozoa. In them it is the normal and characteristic method by which increase in number is brought about. It consists in a division of the cytoplasm

of the animal, preceded by an orderly division of the nucleus. In a few cases, such as *Actinophrys*, it has been possible to make out that there is a mitosis similar to that of metazoan cells, and differing from this only in that the nuclear membrane remains intact. In other cases either the individual chromosomes are too small for it to be certain that longitudinal division takes place, or the constancy of their number has not been established, but since there is general resemblance to mitosis the process is regarded as a reduced form of this and is called cryptomitosis. True amitosis is only universally admitted for the meganucleus of the Ciliophora, and even this it is possible to regard as the last stage of degeneration.

When fission results in the existence of two daughter individuals each about half the size of the parent it is said to be simple and binary. In some cases there is more than one division before the products separate and start to lead independent existences, so that several small individuals result. This end may be brought about in two ways. In repeated fission there is more than one ordinary binary division in quick succession: an example is *Vorticella*, which produces eight small motile forms by three divisions. In multiple fission there are several divisions of the nucleus so that a syncytial condition is temporarily produced, and then the cytoplasm falls apart round the nuclei. Multiple fission is associated with a peculiar condition of the nucleus known as polyenergic in which several sets of chromosomes appear to be present: when the nucleus divides, these sets separate. Multiple fission always occurs in the formation of spores, and is then called sporulation. Spores, in the strict sense, are the products of reproduction of a zygote (p. 251), so that this type of reproduction is closely comparable to the asexual reproduction of plants. It occurs in many Protozoa, but is best seen in some of the parasitic forms such as *Monocystis* and *Plasmodium*.

Budding is the name given to fission in which one of the products of the division is much smaller than the other. It has no relation to budding in the Metazoa. It occurs, for example, in *Arcella*.

7.12. Fragmentation

Fission is sometimes taken to include not only the divi-

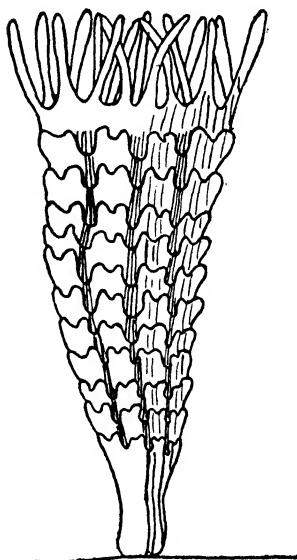


FIG. 38. Scyphistoma of *Aurelia aurita*, dividing transversely to form medusae. The process of division is called strobilation, and the successive medusae which split off from the top and swim away are ephyrae.

sion of the Protozoa, but also all cases where a Metazoon divides into two or more parts without there being any very special structures concerned in the process. For this it is better to use the word 'fragmentation'. *Hydra* is said occasionally to divide into two, and division of this sort is normal in many other coelenterates. The scyphistoma of jellyfish such as *Aurelia* produces a number of medusae by successive transverse divisions (Fig. 38). Actinozoa such as *Metridium* divide in two longitudinally, and the majority of the corals do the same. In the last case, however, the polyps remain attached, so that a colony is produced. The process nevertheless belongs here, as it is quite distinct from budding.

Fragmentation is also a normal method of reproduction in some oligochaetes, particularly the freshwater families Aeolosomatidae and Naididae, and in some genera of the latter sexual individuals have never been found. Division

takes place at a definite point called a fission zone, which is usually formed at a fairly characteristic level (n segments from the front, where n is approximately constant). This is a region where several new segments are interpolated, and where reconstruction of tissues takes place. Usually

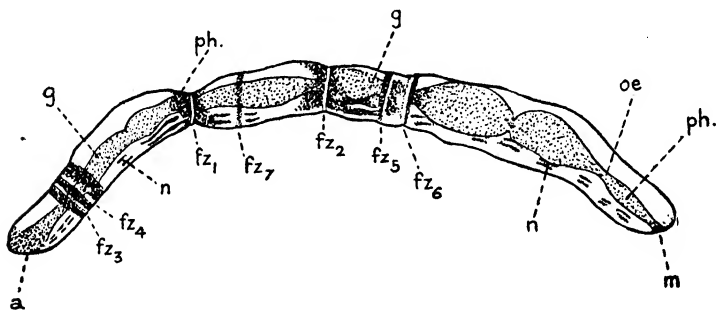


FIG. 39. *Chaetogaster* undergoing asexual multiplication; the general appearance is shown.

Seven fission zones are present; *a.*, anus; *fz.*1-*fz.*7, the fission zones in order of their appearance; *g.*, gut; *m.*, mouth; *n.*, nerve-cord; *oe.*, oesophagus; *ph.*, pharynx. After Wetzel.

the breaking of the animal into two parts does not take place till some reconstruction has occurred, but in some species it precedes even the formation of new segments. In many cases new fission zones appear before fragmentation occurs, so that a chain of as many as eight parts is formed. The whole is co-ordinated and swims as one animal until just before separation (Fig. 39). In many polychaetes fragmentation is used to produce special reproductive individuals which have no function but to swim to the surface of the sea and liberate gametes, so that it alternates with sexual reproduction. An example is the Palolo worm mentioned below in connexion with seasonal spawning (p. 254). In some cases, as in *Nereis*, the reproductive individual is rather different in appearance from the normal, and has been given its own generic name.

The type of protozoan fission called plasmotomy is probably best considered here. It is a division of a multinuclear organism independently of its nuclei, and may be subdivided according to the number and type of the products. It occurs in *Opalina*, where it is binary, and in the Mycetozoa, where it is multiple.

7.13. Gemmation or Budding

Gemmation or budding perhaps corresponds to what botanists call vegetative reproduction, and, as with that process in plants, it may lead primarily either to an increase in the number of individuals or to the production of a colony. It is difficult to separate it formally from fragmentation, but in practice there is seldom likely to be confusion. A bud is much smaller than the parent, is lateral, and is formed as a whole from a small group of embryonic cells. Budding is characteristic of the coelenterates and the ascidians. Lateral buds grow on *Hydra* when the food-supply is good, particularly (in the laboratory) in April and May. Secondary and even tertiary buds may be formed before separation begins. This last process is carried out by the bud seizing on to some solid object with its tentacles, and pulling itself apart from its parent. Except that it may grow one or two more tentacles, and will at the proper season form gonads, the bud at the time of detachment is a perfectly formed *Hydra*. In most of the other coelenterates, whether Hydrozoa or Actinozoa, the buds do not become detached, so that a colony is formed. Budding only occurs occasionally in the Scyphozoa, where the scyphistoma sometimes multiplies in this way.

There are several species of compound ascidians, which bud in different ways. In the larger number of genera, of which *Clavellina* is an example, a hollow median stolon grows out from the ventral side of the abdomen, and on this buds grow. Blood-vessels and other structures grow

into these and are common to the whole colony. In a few genera, such as *Botryllus*, the buds are formed from paired outgrowths of the atrium, and in *Doliolum* the buds are formed at one point, become detached, and then migrate to another place where they become attached again. It is maintained by some workers that in the budding no regard is paid to the germ layers from which the new tissues normally come, but by others this is strenuously denied.

7.2. Sexual Reproduction

The essence of sexual reproduction is that two cells or energids (the distinction between them is for the present purpose immaterial) come together and fuse. The fusing cells are called gametes, the resulting structure is a zygote, and the orderly process by which the cytoplasm of the two mixes and the nuclei become combined to form one is called syngamy. It is also referred to as conjugation, but since this word is used in protozoology in a rather different sense its use in this way is to be avoided. Fertilization is the same thing as syngamy, but the two words are used with slightly different values. Syngamy is generally chosen when the emphasis is on the phenomenon of fusion as a whole, fertilization when the process of fusing is being considered. In fact the slight difference in meaning between fusion and fusing corresponds to that between syngamy and fertilization. Since in some cases one of the gametes may be induced to develop without the other, fertilization is sometimes used with the meaning 'the process whereby one gamete causes another to develop'. The fact that sometimes the nucleus of the fusing cells divides before nuclear fusion takes place but after the two cytoplasms have mixed, makes a formal definition of gametes and of fertilization practically impossible, for in these cases the cytoplasm which fuses is that of a different pair of cells from those to which the fusing nuclei belong.

It is obvious that syngamy by itself leads to a reduction of the number of individuals. By itself, then, it does not lead to a perpetuation of the race unless the gametes exceed in number the parents which produce them. This is normally the case.

It follows from the definition of syngamy as the fusion of two cells that the Protozoa are the only animals in which it can take place between adults. In this phylum there are a few cases of ordinary full-grown individuals fusing, as in *Polytoma*, and the partner which bears all the cytoplasm in the syngamy of ciliates may perhaps be regarded as full-grown: it is certainly full size. Such gametes are called hologametes, and the small specially prepared ones merogametes. Outside protozoology the terms are never used since they are unnecessary.

The Protozoa also differ from the Metazoa in that the two fusing gametes may be both alike so far as the microscope can distinguish. They are then called isogametes. In other cases in the Protozoa, and everywhere outside this phylum, the gametes differ in size or form or both, and are called anisogametes. The smaller may be called simply a microgamete and the larger a megagamete, but more often the one which is small is also more active, and is called a male or a spermatozoon, and the other, large and sluggish, is called a female or an ovum. The first term is often shortened to sperm, and the second translated as egg. At this point, where dimorphism of gametes begins to be developed, sex, as distinct from sexual reproduction, begins. The differentiation of the sexes is another thing still—the existence of two types of adult to produce the two types of gamete. Although primarily the difference need concern only the reproductive organs (such is the case in the coelenterates) it may affect accessory structures, as in the frog, the whole external appearance, as in many birds, or the general mental outlook, as in man. An animal

which produces both male and female gametes is a hermaphrodite. Much has been written about the possible reasons for the existence of sex and sexual reproduction, but since all the alleged explanations are teleological they do not fit into the framework of science as ordinarily understood. Whether true or not, they have no place in a text-book of physiology.

In the Metazoa the preparation of the gametes involves a meiosis, that is a process of cell division in which the chromosomes are reduced to the haploid number. In the Protozoa this is difficult to make out, but it has been observed in widely separated species—in *Actinophrys*, *Paramaecium*, and some amoebas—so that it is probably the normal thing. In most Sporozoa and in the Volvocina meiosis occurs immediately after syngamy, and the animal lives nearly all its life in the haploid state. (This is of course also the case in the gametophyte generation of plants.)

It has been pointed out that conjugation is often used to express something rather different from syngamy. It means the coming together of two Protozoa so that syngamy follows. The case which is most familiar is that of *Paramaecium*. Here two adult individuals unite by their ventral surfaces, and nuclear changes then take place. Finally, one daughter nucleus from the first individual goes across and fuses with a nucleus which has remained in the second individual; meanwhile another nucleus similarly travels from the second to the first. The two motile nuclei may be regarded as male gametes, and the non-motile ones, with their associated cytoplasm, as females. In most Protozoa other than the Ciliophora conjugation consists merely in the ordinary fusion of two gametes, and is therefore synonymous with syngamy, but the name is also applied to plastogamy, a process which occurs in the Mycetozoa and in *Amoeba diploidea*, where two masses of cytoplasm fuse without union of the nuclei.

By far the majority of Metazoa have the sexes separate, and even in those species which are hermaphrodite cross-fertilization is the usual thing. Before fertilization can occur the gametes must be brought together. In many marine animals all that happens is that prodigious numbers of eggs and sperms are shed into the sea, so that, small though the chance of any two individuals meeting may be, in total there are very many unions. That gametes of both sexes are liberated at the same time is ensured by the seasonal rhythm of the animal. The exact reason for this rhythm is unknown, but in a general way it may be related to changes in the environment. The most exact examples of rhythm are the polychaetes called Palolo worms, *Leodice fucata* in the Atlantic and *L. viridis* in the Pacific. They swarm at a very limited period—the last quarter of the October–November moon in *viridis*, and the last quarter of the June–July moon in *fucata*. The worms live in tubes, from which the heads normally protrude. The night before the swarming the animals change their position so that the tails protrude, and as soon as the sunlight touches the water on the morrow the tails break off and swim by themselves to the surface. They emit eggs or sperms from the anterior wound where they broke off from the main body of the worm, and then die. There is also a lunar periodicity in other worms, and in some sea-urchins and molluscs. The reason for this, and even its value, is problematical, since some animals reproduce well enough without it, and a species which has a lunar rhythm in one place may be without it in another. Even Palolo worms from some areas do not swarm, but if those from the swarming areas are kept in the dark in the laboratory, they swarm at the same time as their relatives which have been exposed to the moonlight.

In some species the shedding of gametes is determined by some substance released by the opposite sex. Under

normal circumstances in *Nereis limbata* (an American Atlantic form) several males swim round a female and shed sperms, and she then liberates eggs. If the sexes are confined in the laboratory, the gametes are retained, but the addition of water which has contained females causes the release of sperms, and sperms cause liberation of eggs. It is probable that this type of mechanism is fairly widespread.

Hydra has a variant on this indiscriminate shedding of gametes: the ovum is retained in the body of the parent, but protrudes so that the sperms shed generally into the pond may reach it.

It is only in water where there are no strong currents that this wide release of the two sorts of gametes is likely to be successful. In the tidal zone and in running waters there is usually some more exact conjunction of the two sexes. In the salmon the female scrapes a hole on the river bottom, and lays her eggs in this; the male sheds a cloud of sperms ('milt') over them, and the stream helps to mix the two. Fertilization in the frog is carried out during a sexual embrace called amplexus. The male recognizes the female by the warty skin which she develops in the breeding season, and holds on to her because she is stout. The eggs are laid, and their contact with the symphysis pubis region of the male acts as a stimulus for the emission of his sperm. When all the eggs have been laid the female is much thinner, the stimulus which causes the male to hold her is removed, and she is released.

Sperms are motile by a tail which is in effect a flagellum, and so they cannot live on dry land. Terrestrial animals must therefore have some means of bringing sperms and eggs into contact, and they normally do it by placing the sperms inside the body of the female: the act of doing this is called copulation or coition. Such conjunction of the sexes is also found in some aquatic animals, such as the

cartilaginous fishes and the gastropods. In some cases, as in reptiles and birds, there is no special organ for carrying the sperms, the genital apertures of the two sexes merely being apposed, but in other cases a special intromittent organ, the penis, is present. In the snail this is highly muscular. In mammals it contains erectile tissue which consists of yellow fibres and strands of smooth muscle enclosing spaces in communication with both arteries and veins. The smooth muscle of the organ, and the muscular walls of the arteries, are normally contracted, but in sexual excitement they relax, so that the organ becomes filled with blood and turgid. In this state it is inserted into the vagina of the female, and the semen containing the sperms is ejaculated by contractions of the muscles of the vas deferens and urethra.

In some animals an ordinary part of the body is used to transfer the sperm. In *Octopus*, for instance, a specially modified tentacle, the hectocotylus, places it in the mantle cavity of the female. The male spider sheds a drop of semen on to a leaf, or sometimes on to a small web which he spins specially for the purpose. To this he applies the end of his palp, which has the terminal joint modified to contain a tubular vesicula seminalis. The palp containing the sperms is then inserted into the genital opening of the female. This might almost be called artificial insemination.

7.21. Fertilization

However the gametes are brought near one another, the final act of fertilization can only take place when egg and sperm have come into contact. This depends chiefly on the activity of the sperm. It is characteristic of the male gamete that it is motile, and in nearly all classes of animals it consists of a head containing the nucleus, a short middle piece, and a tail which is simply a flagellum. In general sperms are inactive in the testis, and only start to swim

when they come into the fertilization medium, whether that be the sea as in starfishes or the secretion of the prostate as in mammals. This implies that the medium either contains something which positively activates the sperm, or that it removes an inhibitor. There is definite evidence that substances of the first class exist. The activity of sperms of starfishes, sea-urchins, and many worms is greatly increased by egg water, that is, water in which unripe eggs have been washed. The material concerned is colloidal but not thermolabile; the effects are to some extent interspecific, but individual species show great differences in their reaction. *Echinus esculentus* sperm has its activity increased four times by egg water, while that of *E. miliaris* is scarcely affected. Strychnine, thyroxin (see p. 176), and some other substances have similar effects to egg water, so that it has been suggested that something closely allied to thyroxin is the active principle in this liquid. This is particularly interesting in view of the connexion between the thyroid and the sexual functions in mammals. Perhaps more important still is the effect of thyroxin in raising the basal metabolism of the organism, for in increasing the activity of the sperms it is doing fundamentally the same thing. It seems that sperms are incapable of absorbing food material even when it is available in solution around them. This means that their life is limited and that the more active a sperm is the more rapidly will it use up its fuel reserves and the sooner will it die. Sperms behave like any other cold-blooded organism; their speed of movement increases rapidly with rise of temperature, so that it is easy to show the connexion between activity and span of life by keeping suspensions of sperms at different temperatures. It is found that a given mass of sperms always consume about the same volume of oxygen during their life, whatever that may be; this confirms the suggestion that a sperm dies when its food reserves

are finished. Egg water, however, raises the total oxygen consumption, but this is easily explicable if its active principle alters the mechanism of the break-down of the reserves. There is, however, some evidence which suggests that sperms may become inactivated through autointoxication by waste products. The oxygen consumption is lowered in dense suspensions, even when the medium is well aerated to remove carbon dioxide.

In nature, sperms probably seldom live for more than twenty-four hours after leaving the testis, and fertilizing power is lost sooner than this, but in a few species they are stored in the female for months, or even, as in the honeybee, for years.

Sperms have been described as swimming towards crystals of thyroxin, but there seems to be no evidence of any natural chemotaxis towards the egg in animals comparable with the way in which fern spermatozooids are attracted to the archegonium by malic acid. The mere prodigality in the number of sperms probably ensures that many of them are brought close to an egg. In man the distance which the sperms have to travel to meet the egg in the Fallopian tube, where fertilization occurs, is about 25 cm.; their speed of movement is 2-3 mm./min., so that their journey would take them about two hours, which is well within their life span.

Whether or not the sperm is in any way attracted to the egg while it is swimming freely outside, as soon as it touches the jelly which surrounds the egg it nearly always burrows in normally to the surface. In sea-urchins, as many as thirty sperms may enter the jelly, but it is rare in any species for more than one actually to penetrate the cytoplasm. This may be partly because as soon as one has done so a fertilization membrane forms round the egg, and through this no more sperms can make their way. The formation of this membrane is accompanied in the frog by

the development of an action potential, and it must presumably be an indication of a chemical change in the protoplasm. The egg with a fertilization membrane has (in the sea-urchin *Arbacia*) an oxygen consumption six times what it was before, and there are also changes in its permeability and electrical conductivity. In some cases the fertilization membrane appears to be merely the pre-existing vitelline membrane which has been lifted up and made visible, and in all cases the membrane is only a sign of much more fundamental changes.

7.22. Reproductive Rhythm in Mammals

It has been pointed out above that in animals which liberate their gametes freely into the sea synchronization of the escape of eggs and sperms may be assured by a seasonal rhythm affecting both sexes. It is equally important that in animals with definite conjunction of the sexes, both male and female should be fit for intercourse at the same time. This also is often brought about by a reproductive rhythm which has some connexion with the seasons. The nesting season of birds, the rutting season of many mammals, and the menstrual periods of women are obvious examples which have been known from the earliest times. Within the last few years some progress has been made in elucidating the factors which determine this rhythm. It is convenient to start with mammals, since more is known of them than of the other classes.

The rhythm is most marked in the female. The essential part of the ovary is the Graafian follicle. When this is ripe (Fig. 40) it consists of a vesicle with an outer wall or theca and an inner one called the membrana granulosa. Attached to the latter at one side is a mass of cells, the discus proligerus, which contains the ovum. The cavity of the vesicle contains a fluid, the liquor folliculi. The theca is formed from the general stroma of the ovary, while the membrana

granulosa, discus proligerus, and the ovum itself are developed from the original cubical epithelium on the surface of the foetal ovary. It is improbable that this epithelium sinks in to form any new follicles after birth.

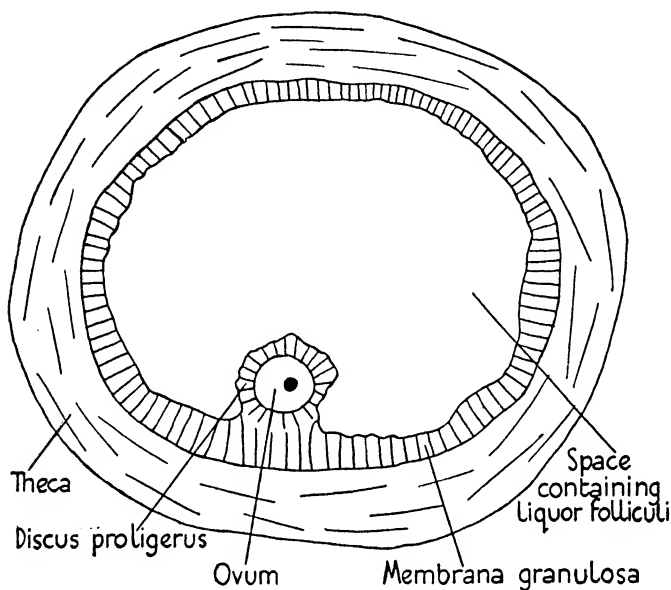


FIG. 40. Section of a nearly ripe Graafian follicle of a rabbit, $\times 125$.

Ovulation consists in the rupture of the follicle and the liberation of the ovum into the body cavity. Only a few follicles burst together; in the rabbit five or six on each side is the normal number, and in the human being but one, the ovaries working alternately.

After ovulation the cells of the membrana granulosa and of the theca increase in size so that in the place of the follicle there is formed a dense mass of cells known as the corpus luteum.

The process of growth and degeneration of the follicle,

with its accompanying changes in other parts of the body, is called the oestrous cycle.

The simplest sexual rhythm in mammals is an annual one, for most wild mammals breed at one season only of the year. Traditionally this is the spring, and with very few exceptions the Insectivora, Carnivora, Rodentia, and non-ruminating ungulates breed about April in the Northern hemisphere, and September in the Southern. In most Artiodactyla, however, the rutting season is the fall. When an animal is moved from one hemisphere to another its breeding season may change so that the animal is still sexually active at a time of increasing or decreasing light intensity, as the case may be. Red deer which have been imported into New Zealand continue to rut in the fall, but this is of course six months different from their time in Europe. Sheep taken from Britain to South Africa have changed similarly, in some cases during their first year in the new home.

The oestrous cycle fits into this annual breeding cycle, but it is not necessarily synchronous with it, for although some animals, such as the fox, are monoestrous, that is have one ovarian cycle in a breeding season, most species are polyoestrous, and have several cycles fitting into the year. There is no essential difference between the two cases, but polyoestrus is best regarded as a secondary rhythm imposed on the main one. There are four phases of the cycle.

1. Dioestrus, a quiescent period when there is no sexual activity. The long period of quiescence between breeding seasons is called the anoestrus.

2. Pro-oestrus, a preparatory phase during which the follicle is developing.

3. Oestrus, the period of heat. At this time there are usually changes of hypertrophy in the external genitalia, and it is only at this time that the female shows any sexual

desire: at other times males are repelled. There are also changes in the walls of the vagina, which become cornified. In the majority of animals ovulation occurs in this period, but the rabbit, ferret, and cat ovulate only after copulation. (This peculiarity of these animals makes them very suitable for research where the exact time relations of subsequent events are required.)

4. After oestrus there is a degenerative postoestrus, but this is generally merged into the state of pregnancy (when fertile union has occurred) or pseudopregnancy (when it has not).

In the rabbit ovulation takes place ten hours after copulation. The half-dozen ova are packed, with some other cells from the follicle, in albumen which clots round them when the liquor folliculi escapes. The mass is carried to the ostium abdominale by the cilia of the body cavity, and it then enters the Fallopian tube, forming a plug at the top of this. By this time the thickest density of the up-swimming sperms has nearly reached the top of the tube, and the chance of fertilization is high. The sperms liberate a protease which dissolves the albumen, so that when the eggs are fertilized they can be carried down the uterus by the cilia of the tube. Fertilization has occurred within sixteen hours from copulation. Division of the egg starts in the Fallopian tube and continues in the uterus. The beginning of the attachment of the foetus to the latter starts on the eighth day.

It is likely that the course of events in other mammals is similar, but the time relations will naturally be different. It would seem that where ovulation takes place without reference to mating the chance of fertilization would be greatly lessened.

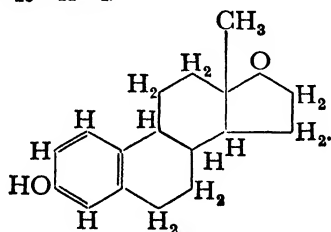
Changes in the endometrium (the lining of the uterus) have begun even before the embryo has arrived, but they become more marked after this. The superficial epithelium

degenerates, and the embryo sinks in against the connective tissue. By a growing together of tissues from both embryo and mother the placenta is formed, and to make the maternal part of this the uterus grows out into villi, and its blood-vessels, particularly the veins, increase greatly in size. As pregnancy continues the uterus increases in size, and its cavity becomes greatly enlarged to hold the developing embryos. The vagina also increases in size. Other changes occur in pregnancy, particularly the development of the mammary glands so that milk can be supplied to the young at, or (in man) a day or two after, birth. In the later stages of pregnancy the animal often behaves differently from the normal by retiring from the herd, making a nest, and so forth. Seals migrate long distances to land for parturition to take place.

Pseudopregnancy is a state which occurs at the end of the oestrous cycle in many mammals when fertilization has not taken place. It consists in the same phenomena as pregnancy, but they are developed to a lesser degree. The changes in the uterus begin, but cannot go to the stage of the formation of the placenta, and there is some enlargement of the mammary glands. The bitch collects material for a bed, and the doe rabbit plucks her fur as she does to shelter her young in the ordinary way. In most mammals, but not in the rat or mouse, dioestrus is simply a short and not very marked pseudopregnancy.

The growth of the Graafian follicles is not itself the factor which determines the other changes, since oestrus occurs when all the follicles have been destroyed by X-radiation. It does not occur, however, if both ovaries are removed in their entirety. It is therefore likely that an oestrus-producing hormone is manufactured by some part of the ovary other than the follicles. Such a hormone was first discovered in extracts of ovaries in 1912, and has since been found in the placenta and in urine of both males and

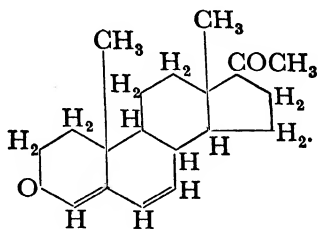
females, but particularly in that of females at about the time of ovulation and when pregnant. Extracts of all these induce oestrus within two days after being injected into spayed mice, but neither the urine nor any organ normally has oestrogenic properties unless either an ovary or a placenta be present. Several substances with oestrogenic properties have now been isolated, such as oestrone, oestriol, oestradiol, equiline, and equilenin: collectively they are known as oestrins, and form a group of closely related sterols of which oestrone will do as an example. Its formula is $C_{18}H_{22}O_2$,



It is unknown which of these is the primary product liberated by the ovary, but oestradiol, which is a dihydro-oestrone, is the most active and it is probable that the others are derived from this. The oestrins are not specific. A number of related synthetic substances have been shown to produce oestrus.

Oestrus is usually followed by pregnancy or pseudopregnancy, and the change-over to this phase is marked by the development of the corpus luteum. In those animals, such as mice, in which there is scarcely any pseudopregnancy, the corpora lutea develop very little and soon degenerate unless copulation occurs. If a female mouse is mated with a sterile male, fertilization cannot occur, but the corpora lutea persist much longer than usual, and there is a marked pseudopregnancy which postpones the onset of the next sexual cycle for seven days. (Normally the

whole cycle only takes five days.) Pregnancy or pseudo-pregnancy is associated with the production by the corpus luteum of a hormone called progesterone (or progestin, or luteosterone) which has the structure



This, in addition to sensitizing the uterus for the attachment of the embryo and producing the characteristic changes in the reproductive organs and mammary glands, also inhibits oestrus and ovulation. It is therefore only when the effects of the corpus luteum have worn off that oestrus can occur again. The corpora lutea are normally necessary for the maintenance of pregnancy, for if they are removed in most animals abortion occurs. In some, however, such as man, horse, cat, and rat, their persistence is not essential, and their function is probably taken over by the placenta itself.

The discovery of oestrin and progesterone gives an immediate cause for oestrus and pregnancy, but it does not fully explain either the rhythm or the first onset of oestrus at puberty and in each annual season. It is now certain that the anterior part of the pituitary gland is at work here. It produces several different hormones (see pp. 180-1), and amongst its actions is one on the reproductive system. Injection of suspensions of the anterior pituitary into adult females causes ovulation, followed, as would be expected, by luteinization (formation of corpora lutea). Similar treatment of immature females leads to a precocious oestrus and ovulation. These effects agree in import with the

entire cessation of sexual activity caused by removal of the pituitary. It is possible that two hormones are produced, one inducing ovulation and oestrus, and the other luteinization, but the matter is not settled. The two have been called APH-A and APH-B respectively. Substances with the trade names Prolan-A and Prolan-B have similar effects, but it is not certain that they are identical with the pituitary hormones.

The interaction of the anterior pituitary and the ovary seems to be mutual, for in castrates the gonadotropic activity of the pituitary increases. Moreover, it can be lowered again by the administration of oestrin.

The cycle may then be pictured as follows (Fig. 41): first, the pituitary produces APH-A, which stimulates the ovary to form oestrin. The latter brings on ovulation and the characteristic phenomena of oestrus, and also reduces the activity of the pituitary. Oestrus is followed by the luteinization as a result of the presence of APH-B. (It is obvious that corpora lutea cannot be formed until ovulation has occurred.) Meanwhile the inhibition of the pituitary by oestrin has removed the stimulus for any further ovulation or production of oestrin, and then with the depressant factor removed the pituitary becomes active again. The ovary is again stimulated to produce oestrin, and a second cycle has begun. Sometimes oestrus and ovulation do not go together, with sterility as the inevitable result.

To make the story reasonably complete we must know the immediate cause of the secretion of gonadotropic hormones by the anterior pituitary, and here the oestrous cycle can be linked up with the longer seasonal cycle. If doe ferrets are exposed to electric light in winter, they come to full heat in 38-64 days, although they are not normally in season until April. It is the visible and particularly the ultra-violet rays which are effective, and similar results

are obtained for a spread or a concentrated dose of the same total magnitude. Hypophysectomized animals (i.e. those in which the anterior pituitary has been extirpated) do not respond. Since one blind ferret did not respond it is likely that the stimulus of light is received by the eyes

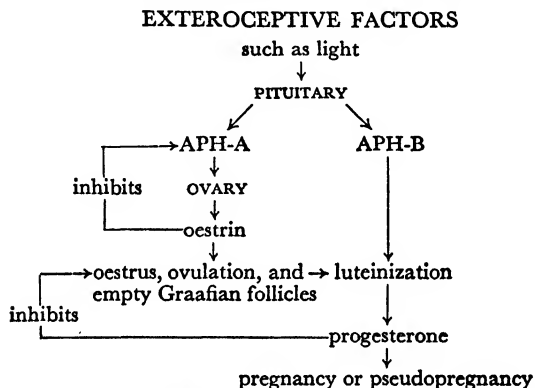


FIG. 41. Schema of the oestrous cycle in mammals.

and transmitted to the pituitary by the central nervous system. Raccoons also have been induced to breed six weeks before their normal time by exposing them to an increased light intensity.

In these experiments the effects of temperature and food were eliminated, but in nature these factors might have some action. Unfortunately experiments on other animals have not given similar results, so that one is scarcely justified in generalizing. It does, however, appear probable that the increasing amount of light in the spring is the general cause of secretion by the anterior pituitary which starts the oestrous cycle. This agrees in general with the times of breeding of mammals, although there are some difficulties.

In domestic animals, such as the cow, which may breed at any time of the year, it seems likely that excess of food

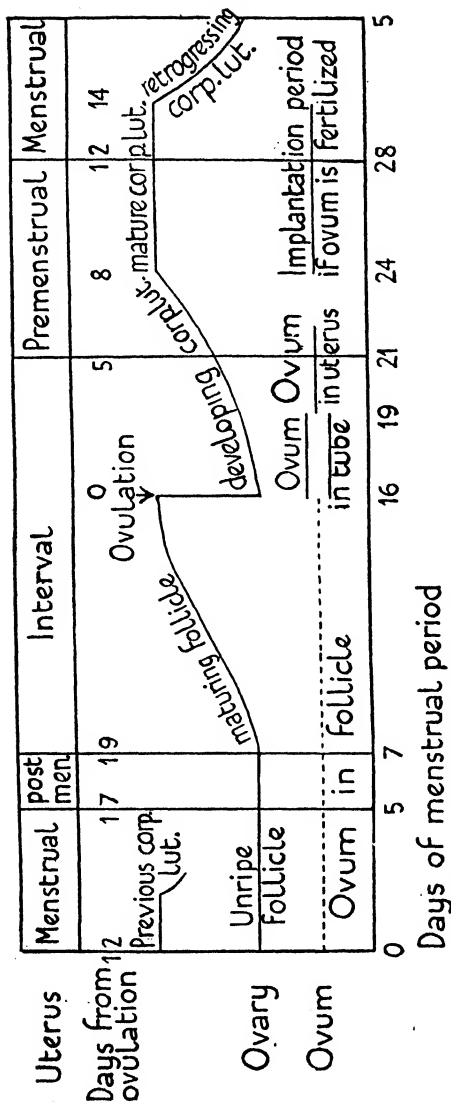
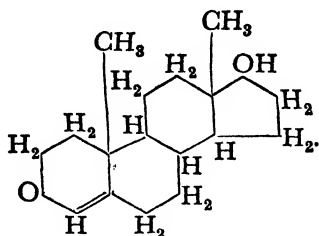


FIG. 42. The relationship of the human menstrual cycle to the normal mammalian cycle. Slightly modified from Corner

or some other factor has eliminated the necessity for light or any other external stimulus to start the cycle in operation. In the Old World monkeys and in man the oestrous cycle appears to be replaced by the menstrual cycle, which is marked by a flow of blood and mucus from the uterus. By investigations on monkeys, together with some evidence from man, it has been shown that the two cycles are closely interlocked. First, there is the interval dominated by oestrin, when the follicle is maturing, leading up to ovulation. During this time the endometrium is unspecialized and thin. After ovulation, a corpus luteum is formed, and progesterone becomes the dominating hormone; under its influence the endometrium thickens and becomes vascular and glandular, the premenstrual period. This represents a preparation for the ovum, and is obviously a condition of pseudopregnancy. When fertilization does not take place the corpus luteum degenerates, and so both hormones are reduced in quantity. As a result of this the endometrium breaks down and the blood and cells resulting are discharged in menstruation. There is a brief postmenstrual period before the next follicle begins to mature. Thus the periods of pro-oestrus and oestrus are represented by the interval, pseudopregnancy by the premenstrual period, and the dioestrus by the menstrual and postmenstrual periods. In the human menstrual cycle ovulation probably occurs between the thirteenth and seventeenth days, counting from the beginning of the menstrual flow (Fig. 42). It must be added that the agreement between the two cycles is not exact, as in monkeys menstruation quite often takes place without ovulation; the proximate cause of menstrual bleeding seems to be a sudden lowering of the amount of oestrin in the blood.

Cyclical changes in the reproductive organs are not so obvious in the male as in the female, but they are nevertheless there. The interstitial cells of the testis produce a

hormone called testosterone which is closely allied to the ovarian hormones; its formula is



(Androsterone is less active and is found only in urine.) Injected into castrated rats testosterone prevents degeneration of the accessory sexual organs—vasa deferentia, prostate gland, &c.—which they would otherwise suffer. Rats castrated before puberty show no sexual behaviour, but if they are injected with a derivative of testosterone their accessory organs develop and they copulate when presented with females. Testosterone is not formed if the anterior pituitary is removed, but hypophysectomized animals do make it if they receive injections of a suspension of the anterior pituitary. Buck ferrets which receive artificial light in winter become sexually interested and their accessory organs develop. The unions are, however, sterile, because spermatogenesis is incomplete. These observations suggest that the male is influenced similarly to the female, but the details of the process are even less well known. There is no evidence that males undergo rhythmic changes similar to the oestrous cycle of females, and there is no reason why they should. The female is only willing to receive the male while she is on heat—that is just about the time of ovulation—and provided that the male is then able to discharge active sperms fertilization is reasonably certain. The case of those animals, such as the rabbit, where ovulation occurs only after coition, may be regarded as a refinement which makes assurance doubly

sure. The mechanism by which ovulation is brought about is obscure, for it takes place even if coition occurs when the vagina and vulva are anaesthetized, the ovaries transplanted, and the sympathetics cut. It can be induced experimentally by the hormone of the anterior pituitary or by strong electrical stimulation of the central nervous system.

7.23. Reproductive Rhythms in Other Vertebrates

The oestrous cycle occurs in mammals only, but birds and Amphibia are influenced seasonally in a very similar way to mammals. The normal breeding season of birds is the spring, and this is the time when days are lengthening. That birds are very sensitive to light is shown by the phenomenon of the dawn chorus—the outburst of song from all species which occurs just before sunrise. The testes of birds are subject to great seasonal variation in size, becoming much larger in the breeding season than at other times. In a number of species, including the starling (*Sturnus vulgaris*), it has been shown that excess of artificial light in winter may bring on a premature swelling of the testes. In *Junco hyemalis*, a Canadian finch, it has been shown that it is not the light itself but the resulting activity which is responsible for the change. Birds are active if they are awake, and they keep awake so long as it is light. Finches were confined in a cage in which a rod on an endless belt moved along the perch at regular short intervals. The birds became quite used to skipping over the bar, but by so doing they were prevented from sleeping. Although they were kept in dim light which was shown by control experiments not to be effective in itself, their testes hypertrophied to the spring size. Similar experiments on starlings caused production of sperms when the length of day reached a certain threshold; this varied, but was about 12½ hours. It is likely that here too activity

is important. The starlings which roost in winter on the National Gallery and nearby buildings are kept awake by the traffic until about midnight, so that their active day is six hours or so longer than that of birds living in more rural districts. Starlings collected from the Trafalgar Square roosts in February were found to have much larger testes or ovaries than country birds at the same time. The light intensity in the London roosts at night is less than that which in control experiments was found to have no effect.

It is likely then that the breeding season in birds is mainly determined by activity, which in turn bears a direct relation to the amount of light. Anterior pituitary extract induces broodiness in fowls, so that it is possible that the activity acts through this gland. Undoubtedly other factors are important, for in cold weather the mating behaviour in male moorhens (*Gallinula chloropus*) is interfered with and may even stop altogether.

It has been maintained that an ecological factor, the date at which nesting sites become available, cuts across climatic factors, but this can only work within the limits set by the functional activity of the gonads. It is difficult to apply the mechanism of light-induced activity to the breeding season of tropical birds, but there is some evidence that changes in the intensity of visible and ultra-violet radiation may be important. The final coming together of the sexes is a result of sexual display in which both cock and hen take part. (Courtship is a bad word, since the behaviour to which the name is given usually takes place after partners have been selected.) In a bird such as the moorhen there is a series of behaviour patterns in the two sexes, ending in coition. Presumably the display acts by stimulating the anterior pituitary; in other words it is an aphrodisiac leading to synchronization of orgasm. The degree to which birds are dependent on this

sort of stimulation varies with the species. The barndoor fowl lays eggs throughout the year whether cocks are present or not, but pigeons will only lay eggs after mating. Here it is presumably merely the sight of another individual which is the stimulus, for if two hen pigeons are confined together they may both lay eggs. The period over which sexual activity is maintained depends on the subsequent behaviour of the bird. Normally one nest is built, and a characteristic number of eggs are laid; if the nest is destroyed, another will be built, and if the eggs are removed as they are laid far more than the normal number will be produced. The house-sparrow (*Passer domesticus*), for instance, normally lays a clutch of four or five, but it has been induced to lay as many as fifty.

Most of the work on Amphibia has been done on *Xenopus laevis*, the clawed toad of South Africa. It is a tailless species in general similar to the common frog, but the mating embrace is lumbar instead of axillary, that is to say the male clasps the female round her waist, in the region of the urostyle. In the laboratory these animals show no sexual behaviour even if they are brought in during the mating season. Amplexus can, however, be induced at any time by injections of anterior pituitary extract. Ovulation follows, and the larvae from the unions have been reared through to a late tadpole stage. In the female, anterior pituitary extract can be replaced by progesterone, and in some cases this will induce mating and ovulation even in hypophysectomized or immature individuals. It is therefore probable that the pituitary is as important in the sexual life of Amphibia as in that of mammals and birds. Since artificial sunlight in December makes frogs try to spawn it is probable that light is again the important climatic factor. The pituitary hormone is not specific, for implantation of the anterior pituitary of

the frog into immature female mice activates the reproductive organs.

7.24. Hermaphroditism

An animal which produces both male and female gametes is called a hermaphrodite. In many of the Protozoa, such as *Paramecium*, hermaphroditism may perhaps be primitive, but in the majority of animals in which it occurs it seems to have some connexion with the environment, for it is common in parasites and in the freshwater and terrestrial forms of some groups, but is rare in the sea. It is obvious that in parasites and in animals living in small isolated ponds hermaphroditism accompanied by self-fertilization would greatly increase the chance of the production of offspring, and might therefore have been evolved by natural selection, but in fact self-fertilization is rare, and ova and sperms are not usually produced at the same time. An animal which forms first sperms and then ova is protandrous, and if the order is reversed it is protogynous. In many animals, such as the snail and the earthworm, this alternation of sex is seasonal, but in some others there is no retrogression to the original sex once the change has taken place. In these cases the term hermaphrodite is not very appropriate, as there is just one very real, though perhaps slow, change of sex during the life-history. The best-known example is the mollusc *Crepidula fornicata*, the slipper limpet. The larvae of this are male when newly hatched, but if they settle down on the floor of the sea they become females. Others settle on top of them, produce sperms, and fertilize the females below. After a time these males begin to change their sex, and other males settle on their backs. This goes on till a pile of half a dozen or more molluscs is formed, those at the bottom being females, those in the middle hermaphrodite, and those on top males, of which the later ones are waiting for the animal

below to change its sex. Each individual is at first male, then hermaphrodite, and finally female, with the exception of the first in a chain, which is female only, and the last, which is male only.

This type of sex reversal is probably similar to that which sometimes occurs in vertebrates. An occasional hen has become a potent cock, and development of the secondary sexual characters of a cock is frequent in old hens. Whatever the exact mechanism of the determination of sex in vertebrates, the line between male and female is a thin one, and intersexes, with some of the attributes of both sexes, are not uncommon. They occur occasionally in man, and regularly in the toad, where Bidder's organ, at the anterior end of the testis, is probably a rudimentary ovary.

7.25. Parthenogenesis

Parthenogenesis is the reproduction which occurs when a cell which appears by its origin and structure to be a gamete develops without fertilization. By our previous formal definitions it is therefore a type of asexual reproduction, but the morphological evidence, that it derived from ordinary sexual reproduction is too strong to be ignored. It follows from what has been said above about the limited life of sperms that it is very improbable that a male gamete could develop parthenogenetically, and in fact it is only in a few Protozoa, such as *Actinophrys*, where the distinction between the gametes is slight, that one ever does.

In a very few animals, such as some rotifers and some species of wasps and sawflies (Hymenoptera), parthenogenesis is the only known form of reproduction, and no males are known. More usually it alternates with typical sexual reproduction, but the degree to which it replaces this and the regularity of the alternation vary considerably. Probably in the majority of cases the alternation is quite irregular. In *Paramecium* and some other ciliates the good

effects of conjugation on a culture can be replaced by those of endomixis, a special sort of parthenogenesis in which in a single individual the meganucleus and much of the

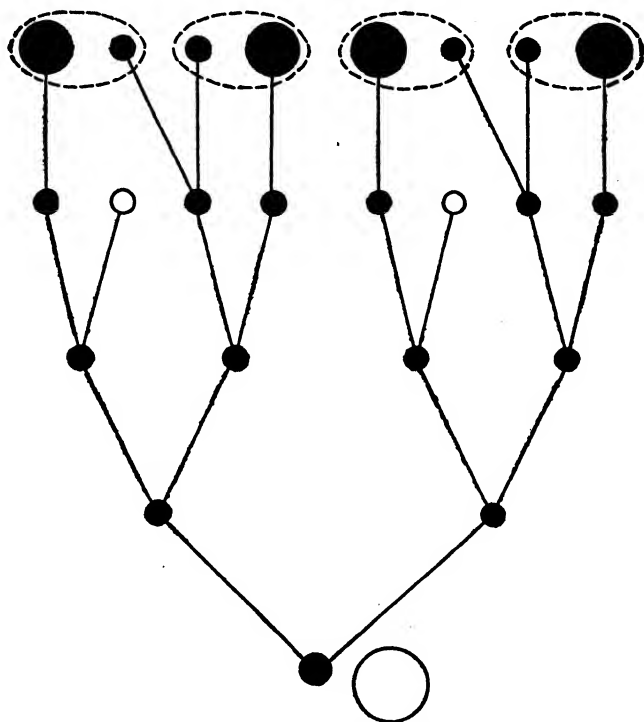


FIG. 43. Diagram of the behaviour of the nuclei at endomixis in *Paramecium caudatum*. White circles indicate nuclei which disappear.

micronuclear material are destroyed just as they are at conjugation. The details of the nuclear division and reconstruction vary, but one scheme is shown in Fig. 43. The frequency with which endomixis and conjugation occur depends in part on the genetic nature of the stock, in part on external factors such as temperature, and in part on the time measured in asexual generations from the pre-

vious endomixis or conjugation. In bugs of the family Aphidae the wingless females which hatch in spring from the eggs which have survived the winter reproduce parthenogenetically, and several similar wingless parthenogenetic generations, all females, follow. Finally in autumn winged females and males are produced, and together they give rise to fertilized eggs which survive the winter and begin the cycle again. There is no constancy in the number of parthenogenetic generations, and the production of males and winged females appears to be connected with falling temperature or shortage of food or both. The Cladocera such as *Daphnia* and many rotifers are similar.

In some insects (Cynipidae or gall-wasps) there is a regular alternation. For example, the individuals of *Neuropterus lenticularis* which appear in March are all females. They lay parthenogenetic eggs in buds of the oak, and in the galls so formed the larvae of the next generation develop. The imagines which emerge from the galls in June are very different from their parents, and were formerly designated by a different generic name. Some are male, some female, and between them they produce fertilized eggs which are laid in oak leaves. The pupae remain in galls on the dead leaves until the following spring, when they come out as the next parthenogenetic generation.

Lastly, in the bees parthenogenesis is facultative, that is, it appears to be under the control of the female laying the eggs. The queen (the female) copulates only once in her lifetime, and stores sperms in a receptaculum seminis for months or in a few cases years. Only if the eggs are to be fertilized are sperms allowed to escape on to them as they are laid.

It is obvious that in the absence of any special arrangement parthenogenesis would mean a halving of the chromosome number in each generation. The details of the methods by which this is avoided are matters for a text-book

of cytology, but it may be said here that almost all the ways conceivable by man are used by some animal or other. In Crustacea and aphids only one polar body is given off at maturation, and there is no reduction division; in bees the eggs are formed normally, but those which develop without fertilization all form males and there is no reduction in spermatogenesis.

Paedogenesis is the name applied to parthenogenesis when it occurs in a larval form. It is found in Cecidomyidae (Diptera) such as *Miastor*. It should strictly be distinguished from neoteny, which is ordinary sexual reproduction by a larva.

VIII

THE ANIMAL IN RELATION TO ITS ENVIRONMENT: REGULATION

MANY factors of the inorganic world affect the life of animals, some of the chief being: concentration of chemical substances, particularly oxygen, water, the hydrogen ion, and metallic cations; osmotic pressure; temperature; light intensity. A full account of the relationship between these and animals belongs not to physiology but to ecology, but the changes which alterations in the environment produce in the animal itself rather than in its behaviour may properly be considered in this book. Particular examples of such changes have been mentioned in the sections on effectors and behaviour, and the present chapter deals only with the means by which an animal makes itself to some extent independent of its environment, that is, by which it regulates. The story of organic evolution is to a great extent one of increasing independence; whereas Protozoa are greatly affected by nearly all the factors listed above, mammals can stand considerable variations in all except oxygen.

8.1. Hydrogen-ion Concentration

The more primitive animals are very sensitive to changes in acidity, but all animals which possess a body fluid, that is, all the coelomates, maintain an internal environment of approximately constant hydrogen-ion concentration, and they do this by exactly the same method as is used by the biochemist in the laboratory. Any acid will act as a buffer; that is, if its degree of dissociation (γ) is plotted against the pH of the corresponding solution (\ast) a curve of the type shown in Fig. 44 is given. Along the straight part of the curve a big change in degree of dissociation corresponds

to a small change in pH. If hydrogen ions (in the form of another acid) are added to the solution, they will, by the law of mass action, drive back the dissociation of the acid originally present, and along the straight part of the curve they must do this to a considerable extent before

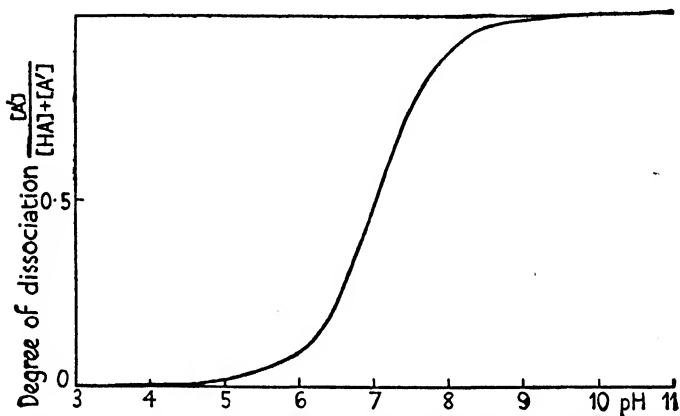


FIG. 44. Graph relating the dissociation of an acid of dissociation constant 10^{-7} to the pH of the resulting solution. Such an acid will act as a buffer between pH 6.5 and 7.5. Other acids will give similar curves shifted either to the right or to the left according to the value of the dissociation constant.

the final pH is very much altered. The solution thus resists change of pH, and is said to be buffered. The position of the straight part of the curve depends on the particular acid used, the hydrogen-ion concentration corresponding to its mid-point being numerically equal to the dissociation constant. Thus acetic acid, with a dissociation constant of 10^{-7} , buffers best at a hydrogen-ion concentration of 10^{-7} , i.e. at pH 7, and is effective from about pH 6.5 to pH 7.5. The degree of dissociation corresponding to the middle of the straight part of the curve may be obtained by adding a salt of the acid, which depresses the ionization in the usual way. It is customary, but incorrect, to name the buffer by the salt. Strong acids are

not considered as buffers, because their dissociation constant is very high, and so they only work in very high concentration of hydrogen ion where buffering is seldom important.

Since the product of the concentrations of hydron and hydroxyl is constant, a similar argument to the above can be applied to bases.

All animals buffer their blood and other fluids by proteins, carbonate, and phosphate. The normal pH varies as between different animals, but is usually between 7 and 8.

8.2. Water

Water is an essential food, and it is obvious that animals cannot become independent of an external supply, but the embryo has in certain cases managed to do so. This is best shown by the vertebrates, which become better at storing water as the evolutionary scale is ascended. In the development of Amphibia and fish a considerable amount of water is absorbed by the embryo from the environment, in addition to that which is obtained from the yolk and by combustion; for example, in the trout (*Salmo fario*) the yolk supplies 59 mgm. of water for the embryo up to the time when it can absorb water through the gut, and 71 mgm. have been taken in from outside. In the reptiles less than one-third of the total water inside the shell at hatching has been absorbed from outside, for the egg has a coating of albumen, and much is got from this. The sole function of the white is in fact to store water. The birds have gone farther: their egg is shut off from the outside by a wall through which water travels slowly; the egg is termed cleidoic. The embryo derives all the water needed for development from the materials already in the egg—from the yolk, from combustion, but chiefly from the albumen. In fact, the eggs actually lose some water during development, and fail to develop unless they do. The

mammals derive the water required during development from the mother.

Most invertebrate eggs absorb water from outside during development, as the fish and Amphibia do, but some of the insects may be independent.

It has been suggested that the development of the cleidoic egg has had far-reaching effects on the nitrogen metabolism. It has been pointed out in chapter II that the exogenous nitrogen in most invertebrates is excreted in the form of ammonia, but that in vertebrates it is either in the form of urea or uric acid, and that these animals can be divided into the fish, Amphibia, Chelonia, and mammals, which are ureotelic, and the birds and other reptiles, which are uricotelic. This distinction corresponds to the one just described between those animals whose embryos take in water from outside, and those which carry it with them in white of egg. The cleidoic egg, which is laid on land, has no means of getting rid of soluble waste products, and if all the nitrogen which would be excreted during embryonic life were to accumulate inside the shell as urea, the concentration reached would almost certainly be toxic. It was a condition of the evolution of the cleidoic and terrestrial egg that uric acid, which is insoluble, should be formed instead. For this to be the case it was necessary that uricase, the enzyme which in most ureotelic organisms destroys uric acid, should be lost. The uricotelic vertebrates have also lost arginase and the power to carry out the ornithine cycle.

Parallel with the change in the chief form of excretory nitrogen has gone a change in the material oxidized to provide energy for the embryo. In fish and Amphibia it is chiefly—up to 90 per cent.—protein. In the chick over 90 per cent. is fat. The advantages of this in the cleidoic egg are that more water is provided per gram of material burnt, and that less waste nitrogen is formed.

Mammals are ureotelic; they have solved the problem of terrestrial life by viviparity; they presumably arose from reptiles which still laid their eggs in damp places and had not developed uricotely.

It must be added that not all physiologists regard this explanation of the origin of uricotely as the true one. It is pointed out that urea is not really very toxic, and that the cleidoic egg of the elasmobranchs, which excrete urea in both embryo and adult, remains unexplained. The alternative explanation for the uricotely of birds and reptiles (and insects) is that it saves water, and so is an adaptation to arid terrestrial life. Uric acid forms supersaturated solutions, from which it separates as an almost insoluble solid; the way in which water is saved by this in birds and insects is described in section 2.55. The shell of the cleidoic egg is merely an additional method of saving water. The elasmobranchs have taken to keeping urea in the blood in order to raise its osmotic pressure (see below). The cleidoic egg is in their case an adaptation to this—the egg is closed so that the urea can be retained, and the egg develops under conditions similar to those in the adult.

8.3. Osmotic Pressure

All living membranes seem to be semipermeable, or, to be more accurate, they have differential permeability for water and solutes. Consequently, no tissue can be in equilibrium with its surroundings unless the osmotic pressures inside and outside are the same. This is the case in most marine invertebrates. The depression of the freezing-point (Δ) of sea-water is 2.0°C. , and that of the blood and body fluids of invertebrates which live in the sea is about the same: they are said to be isosmotic with sea-water. As the salinity of sea-water varies (it is lower, for instance, in estuaries and other places where much fresh water comes in), so does the osmotic pressure of their blood. They

cannot regulate, and are said to be stenohaline or poikil-osmotic. The Chondrostei are similar, but whereas in invertebrates the internal osmotic pressure of the body fluids is maintained largely by the very ions present in sea-water, in these fish it is largely produced by urea. An excretory product has here been put to a good use, and, as has just been pointed out above, it is found even in the egg, and possibly the cleidoic egg has been evolved to make this possible.

In the animals which have been considered so far, regulation is not necessary because their body fluids are in osmotic equilibrium with the surrounding medium, and they are subject to little variation of the latter. There are other groups of animals, called euryhaline or homoiosmotic, which maintain a constant internal osmotic pressure whatever the outside conditions. In the marine teleosts the depression of the freezing-point of the blood is about 0.8°C ., less than half that of sea-water. Either their membranes must be impermeable, and this is not likely to be the case, or they must be continually doing work to prevent or counteract the continual loss of water and resulting concentration of the blood. The second of these alternatives has been shown to be true. To make up for the water which escapes they drink sea-water and absorb it, and get rid of the excess salts which are thus passed into the body by excreting them back into the sea through special cells on the gills. The kidneys secrete small quantities of urine which is isotonic with the blood, so that very little water is lost in that way. It is probable that the cartilaginous fishes can act similarly, although they will seldom need to do so.

Many invertebrates which live in estuaries or in brackish water, where the salinity varies with the rainfall or the state of the tides, are euryhaline. The shore-crab, *Carcinus moenas*, can regulate to some extent. If it is placed in

water which is hypertonic to sea-water (a position in which it is never likely to be situated in nature) the osmotic pressure of its blood follows that of the water, but if the external medium is hypotonic to the sea, the osmotic pressure of the blood is something between its normal value and that of the new medium. The crab can hardly be called homoiosmotic, since there is considerable variation, but it is able to maintain its blood at a different pressure from the medium. It does this by secreting excess water through the gills and antennary gland. Other species which act in the same way are the flatworm *Gunda ulvae*, and the polychaete *Nereis diversicolor*. In both these the first obvious effect of their being placed in dilute sea-water is that they swell; this means that they have absorbed water, but they do not do this to as great an extent as they would if their walls were non-living membranes. It has been shown that as they swell their oxygen consumption goes up, so that presumably a 'respiratory pump' is at work supplying energy to keep the animal in equilibrium (Table 5). This is confirmed by the fact that in the presence of cyanide, which is a respiratory poison, *Nereis* swells passively and cannot regulate. The chief way in

TABLE 5

Oxygen Consumption and Water Absorption of Nereis diversicolor in Dilute Sea-water. Two Specimens were used for each Length of Time. (From Beadle)

<i>Time in hours in 25 per cent. sea-water</i>	<i>Percentage increase in weight</i>	<i>Percentage increase in respiratory rate</i>	<i>Percentage of sea- water equivalent to body fluid</i>
4·25	47	32	55
4·25	54	26	54
22·25	87	42	37
22·25	135	0	38
50·75	74	136	38
50·75	35	26	42

which this energy is used is apparently in driving a hypotonic fluid out through the nephridia. The animal is thus taking up pure water and losing water with some salts in solution, so that its body fluids become diluted. Their osmotic pressure, however, does not fall to that of the external medium. The concentration of the coelomic fluid of a worm which has been placed in 25 per cent. sea-water and allowed to come to equilibrium is the same as that of 55 per cent. sea-water, and comparable values are given for other strengths, but the more dilute the surrounding medium the greater the discrepancy. A full complement of the cations normally present in the sea is necessary for regulation to go on. In *Gunda* the water which is absorbed goes first into the parenchyma, and then into the gut cells, where it forms vacuoles in which it remains.

The body fluids of all animals living in fresh water have a higher osmotic pressure than the medium. The depression of the freezing-point of natural fresh waters varies, but is in general about 0.003°C . Characteristic values for the blood of the animals inhabiting it are:

	$\Delta^{\circ}\text{C}$.
<i>Anodon</i>	0.09
<i>Astacus fluviatilis</i>	0.8
<i>Salmo fario</i>	0.5

All these animals will tend to absorb water from their surroundings and, to prevent oedema, must have some means of excreting it. The Protozoa do this through the contractile vacuole. This organelle is absent from most marine forms, and in *Paramecium* and several other ciliates it has been shown that its rate of pulsation bears an inverse relation to the osmotic pressure of the external medium. There is, therefore, little doubt that its chief job is to act as an osmotic regulator, and the excretory function commonly attributed to it is very small (see pp. 70-1). In most other animals the regulation is largely done by the

excretory organ. In the Turbellaria the nephridia are probably used; they are absent from the marine Acoela, and the rate of pulsation of the terminal vesicle in cercariae goes down as the external osmotic pressure increases. In *Astacus* the antennary gland excretes a urine which is hypotonic to the blood. It is interesting to compare the structure of the gland in this animal with that in the closely related marine lobster, *Homarus*. In the crayfish the coelomic part, which is probably concerned with filtering, and the absorbing tubule are large, whereas in the lobster the resorbing tubule is almost missing, but the labyrinth, which is probably secretory, is large. This distinction holds fairly generally for the marine and freshwater arthropods, and a similar one applies to some other phyla.

In the vertebrates the excess water is excreted through the kidneys, and in freshwater teleosts and Amphibia the glomerulus is well developed, presumably for this purpose. Other mechanisms are at work too, particularly a reduced permeability of the skin. In a pithed frog the excretion of water goes up five times, suggesting that the permeability of the skin is decreased by the action of the nervous system. Excretion can also be raised by the action of pituitrin. In the eel *Anguilla* the gills, which in sea-water are freely permeable and excrete chlorides, &c., to maintain the osmotic pressure of the blood lower than that of the medium, in fresh water become impermeable to both chloride and water. This probably makes it easy for the fish to pass from the sea to fresh water.

It does not follow that because a freshwater animal is homoiosmotic it can be put straight into the sea without taking any harm, any more than a homoiothermic animal can be placed without harm in ice-cold water. It can, however, withstand slight changes of external osmotic pressure, and even fairly large ones if they are made

gradually. The advantage of a constant internal environment is that the metabolic processes of the animal are not upset by sudden variations in the concentrations of ions present.

The ability to regulate may be a property which the animal carries with it from the egg up, or it may be acquired during ontogeny. The fish are examples of the first. There is no appreciable change in the depression of the freezing-point of tissues of *Salmo* from the eggs in the oviduct through all the embryonic stages up to the blood of an adult. The Amphibia (frog, toad, newt) are different. The egg in the oviduct has a depression of the freezing-point of 0.48°C ., about that of the blood of the adult, but on fertilization it drops to 0.045°C . It rises during development, rapidly at first, and more slowly after gastrulation. The pronephros is active well before hatching, so that perhaps regulation develops as an organ for carrying it out is formed. Amphibian eggs will not develop in water isosmotic with the serum of the adult. Cladoceran eggs are similar to those of the frog, showing a fall of osmotic pressure on fertilization and a subsequent gradual rise.

8.4. Temperature

In the majority of animals the body temperature is not greatly different from that of their surroundings, and so the rate of respiration (apart from specially stimulated activity) depends on the latter. Figs. 45 and 46 show this. The temperature of the lizards is almost the same as that of their surroundings, and their carbon dioxide production corresponds. Such animals are called cold-blooded or poikilothermic. They are handicapped by both low and high temperatures. In the former their activity is greatly slowed down, and in the latter they have no means of preventing themselves from becoming overheated and so dying. It has been shown that American insects and reptiles

which normally live in deserts where the surface temperature is above 50°C . cannot survive this in the laboratory for more than a few minutes, and they rapidly die if

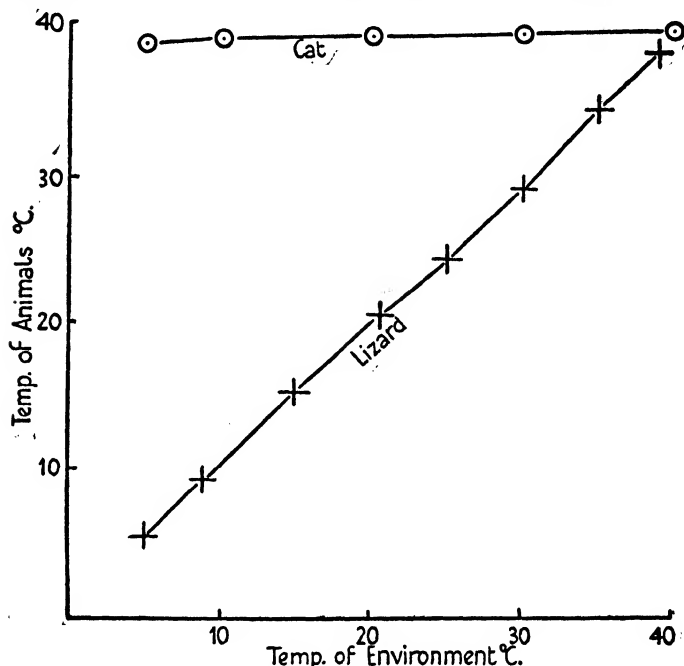


FIG. 45. Body temperatures of cat and lizard (*Cyclodus gigas*) in different environmental temperatures. Redrawn from Martin.

they are tethered in the sun in their natural habitat. In ordinary circumstances they escape by burrowing, and are only occasionally exposed to the temperatures measured by the thermometer.

Birds and mammals are warm-blooded or homoiothermic. Their resting metabolism, that is their energy production irrespective of exercise, goes up as the temperature goes down, in such a way as to keep their body

temperature constant. They are in fact living thermostats. The actual temperature maintained depends on the species, and is subject to slight variation with the individual and with activity. Fig. 45 shows the effect of varying environmental temperatures on the body temperature of the cat. The body temperature remains approximately constant. The graphs in Fig. 46 show that the different behaviour of the cat and of the lizard is correlated with an increased carbon dioxide production at the lower temperatures in the former; at 35° C. the regulating mechanism is beginning to break down. The chief seat of the increased respiration is the muscles, and in the extreme case this is obvious when shivering takes place. The mechanism is dependent on the nervous system, since animals paralysed with curare behave like lizards or any other cold-blooded animals. This type of regulation is called chemical, and can deal only with a lowered external temperature, but there is another type, rather badly called physical, which adapts its possessor to higher temperatures than normal by control of heat loss. This takes different forms. In man, of the total heat produced 5 per cent. goes in heating food, drink, and respired air, 15 per cent. in evaporating water from the lungs, and the rest in cooling and evaporation from the skin. When the external temperature is increased, or when as a result of exercise more heat is produced, the rate of heat loss is raised in two ways. The cutaneous blood-vessels are dilated so that heat is taken to the surface more rapidly, and the sweat glands are activated so that evaporation is increased. Both these are under the control of the central nervous system. In mammals other than man and the Equidae the chief regulation at high temperatures is by tachypnoea—breathing by rapid short pants which evaporate water from the mouth and bronchi, but have little effect on oxygen uptake. Most people have seen dogs breathing in this way after exercise.

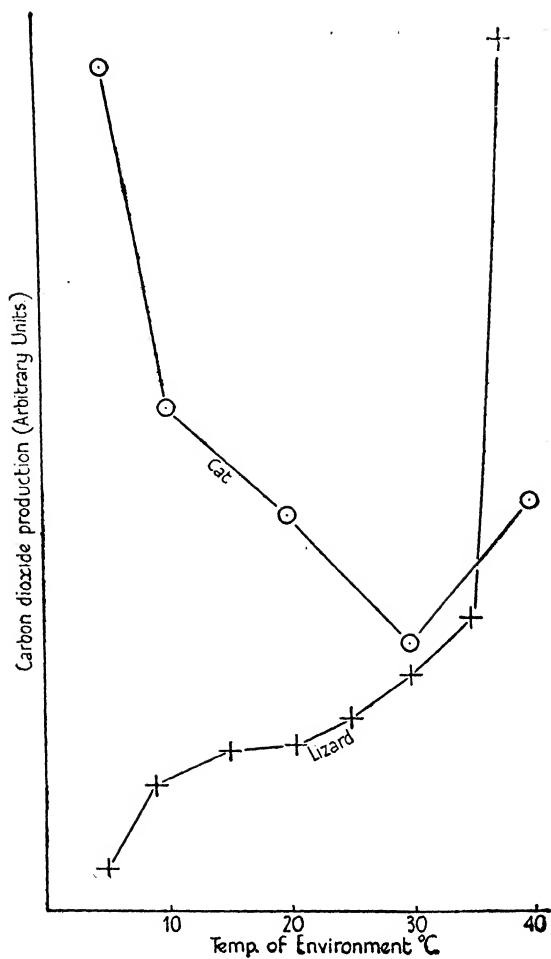


FIG. 46. Carbon dioxide production of cat and lizard at different environmental temperatures. Cf. Fig. 45. Redrawn from Martin.

Homoiothermicity is acquired at some definite point in ontogeny, and the chemical and physical mechanisms arise independently. Not many species have been investigated, but the variation shown at birth is illustrated by Table 6.

TABLE 6

Showing the Forms of Temperature Regulation present at Birth or Hatching. (From Needham)

	Chemical	Physical
Guinea-pig . . .	+	+
Rabbit . . .	+	—
Mouse . . .	—	—
Cat . . .	+	—
Man . . .	+	—
Chick . . .	+	+
Pigeon . . .	—	—

The mammals which can regulate at birth are those which are born open-eyed and active, and similarly the birds which can regulate on hatching are those which are nidifugous, that is which leave the nest as soon as they have broken the shell. Mammals which are born naked and blind are cold-blooded until some days later, when they begin to be more active, and so, likewise, are nidicolous birds, which remain in the nest for some time after hatching. The acquirement of the ability to regulate is not quite sudden, as there is a short period when the homoiothermicity is imperfect.

A certain amount of regulation by evaporation inevitably takes place even in cold-blooded terrestrial animals, and in animals living in deserts it is probably very important. In many of the social Hymenoptera there is some communal regulation by such methods as opening or closing the nest entrances, and fanning with the wings. In the honey-bee in summer there is apparently some

chemical regulation, similar to that of mammals, but it seems to be imperfect.

A special problem which may conveniently be put here is that of hibernation. In winter practically all poikilotherms which are unable to migrate from the cold regions hibernate, that is, they cease moving, feeding, and other activities, and live quiescent with a very low metabolic rate. The temperature at which hibernation sets in varies; usually it is a little above zero, though the pond-snail *Planorbis* is active under the ice. In winter, also, many mammals, particularly bats and rodents, become poikilothermic and go to sleep. At the same time their oxygen consumption falls very low—in the dormouse, *Muscardinus avellanarius*, from a resting value of 8,000 c.c. oxygen per kilogram per hour, to 300. The simplest explanation of hibernation in both cold- and warm-blooded animals would be that the low temperature induced sleep and its accompaniments, but this cannot be a complete explanation. The marmots of North America hibernate in their burrows and their body temperature follows that of the surroundings, which is usually about 2° C. If it rises to 15° C. they wake up, and their temperature rapidly goes up to its normal value of 32° C., but exactly the same thing happens if the external temperature drops to freezing-point. Further, aestivation, sleeping in summer, appears to be very similar to hibernation, and hibernating animals such as dormice and marmots sometimes aestivate. In insects and snails desiccation induces hibernation, and it is likely that it is a common contributory cause in the natural state, but it is difficult to see how it could work for freshwater animals, many of which hibernate. Specimens of the African insectivore *Centetes ecaudatus* at the London Zoological Gardens hibernated at the same time each year, quite irrespective of the environmental conditions. It seems that hibernation is fundamentally a way of avoiding

the ill effects of low temperatures, but that other factors are concerned in producing it. It is in a sense the very opposite of regulation. The whole physiology of the animal is modified while it goes on. Not only is the oxygen consumption reduced, but the type of metabolism is changed so that very little carbon dioxide is formed and the respiratory quotient is low. The potato-beetle, which is normally positively phototactic and negatively geotactic, reverses these taxes on drying so that it burrows to hibernate. Hibernating bats roll over if they are placed on their backs, although this is a reflex which they do not normally possess.

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